



# RHEUMATOLOGY

A patient with rheumatoid arthritis has the following full blood count results: haemoglobin 11.4 g/dl, platelets  $470 \times 10^9/l$  (normal range  $150-400 \times 10^9/l$ ), white cell count  $9 \times 10^9/l$  ( $4-11 \times 10^9/l$ ), mean corpuscular volume 102 fl (80-96 fl).

Which drug therapy is most likely to be responsible for this picture?

A	Leflunomide
B	Methotrexate
C	Ciclosporin
D	Myocrisin
E	Hydroxychloroquine

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# Explanation

## Methotrexate and macrocytic anaemia

In macrocytic anaemia the red cells are abnormally large – the mean corpuscular volume (MCV) is  $> 96$  fl. Antifolate drug therapy, especially with dihydrofolate reductase inhibitors (eg methotrexate, pyrimethamine) causes macrocytic anaemia.

A 35-year-old woman presents with increasing headache, nausea, vertigo, decreasing vision in both eyes and persistent fever. She also complains of pain in her legs when she goes jogging. Her blood pressure is 190/110 mmHg and her femoral pulses are weak, with a radio-femoral delay.

What is the most likely diagnosis?

A	Wegener's granulomatosis
B	Coarctation of aorta
C	Giant-cell arteritis
D	Polyarteritis nodosa
E	Takayasu's arteritis



# Takayasu's arteritis

Takayasu's arteritis is a chronic inflammatory granulomatous panarteritis of the major arteries – the carotid, innominate and subclavian arteries and the ascending arch of the aorta. The brachial, radial and ulnar arteries can also be involved. It most commonly affects women (the ratio of women to men is 8:1), with a typical age onset of 25-30 years. Although it has a worldwide distribution, it is most common in Asia. The usual presentation is with claudication and systemic symptoms of fever, arthralgia and weight loss.

## Differential diagnosis

- + Wegener's granulomatosis commonly presents with upper airway involvement (typically epistaxis, nasal crusting and sinusitis), haemoptysis, mucosal ulceration and deafness due to serous otitis media.
- + Giant-cell arteritis is a large-vessel vasculitis that predominantly affects branches of the temporal and ophthalmic arteries. The mean age of onset is 70 years, with a female to male ratio of 4:1. The most important clinical features are headache localised to the temporal or occipital region with scalp tenderness and unilateral visual disturbance due to vasculitis of the posterior ciliary artery, which supplies the optic nerve.
- + Polyarteritis nodosa (PAN) is a necrotising vasculitis. The characteristic presentation is with myalgia, arthralgia, fever and weight loss. Ocular involvement is rare in PAN.
- + Coarctation of the aorta most commonly occurs in the region where the ductus arteriosus joins the aorta, ie at the isthmus, just below the origin of the left subclavian artery. The other features that this patient demonstrates are not usually seen in this condition.

A 22-year-old college student complains of stiffness and low back pain that is worse in the mornings. An X-ray shows obliteration of the sacroiliac joints.

Given the likely clinical diagnosis, what would be the most appropriate treatment for him?

- A Spinal osteotomy
- B Aspirin
- C Bedrest and immobilisation
- D Prednisolone
- E Spinal extension exercises

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## Explanation

### Management of ankylosing spondylitis

People with ankylosing spondylitis should be encouraged to remain active and follow their normal pursuits as far as possible. Spinal extension exercises and regular physiotherapy are most useful. Spinal osteotomy is rarely used to correct deforming kyphosis. Rest and immobilisation are contraindicated as they may lead to muscle wasting, osteoporosis and ankylosis. Prednisolone is not helpful. Ibuprofen is the preferred analgesic for back pain in ankylosing spondylitis.



A 45-year-old orthodox Muslim woman is brought to the Rheumatology Clinic by her husband. On questioning, she complains of pain in most of her joints associated with difficulty in walking and raising her arms. Blood tests show a microcytic hypochromic anaemia with: total calcium 2.04 mmol/l, phosphate 0.35 mmol/l, alkaline phosphatase 546 IU/l, total bilirubin 11 µmol/l, aspartate aminotransferase (AST) 25 IU/l, alanine aminotransferase (ALT) 16 IU/l, albumin 30 g/l. X-rays of the limbs show Looser's zones in the inferior femoral neck on the left side and the right medial femoral shaft.

What is the most likely diagnosis?

A	Hypoparathyroidism
B	Osteomalacia
C	Perimenopausal osteoporosis
D	Osteoarthritis
E	Bony metastases

## Osteomalacia

Osteomalacia is characterised by defective bone mineralisation, bone pain, muscle weakness and pathological fractures. It is relatively rare in developed countries but can be seen in high-risk subgroups such as female Muslim immigrants and elderly housebound people. The low calcium and phosphate and raised alkaline phosphatase levels and the presence of Looser's zones, which are partial fractures without displacement, are pathognomonic.

This condition is commonly due to vitamin D deficiency caused by poor intake, poor sunlight exposure and malabsorption. Hypoparathyroidism is associated with low calcium, raised or normal phosphate and normal alkaline phosphatase levels. In osteoporosis, the values are usually normal.



A 20-year-old man presents with a 4-day history of high spiking pyrexia and arthralgia. On examination he has a maculopapular, salmon-pink rash on his trunk and arms and his distal interphalangeal joints are swollen. Hepatosplenomegaly is present.

What is the most likely diagnosis?

A	Hepatitis C infection
B	Adult Still's disease
C	Infectious mononucleosis
D	Rheumatoid arthritis
E	Behçet's disease

# Explanation

## Adult Still's disease

Adult-onset Still's disease is found worldwide, with an incidence of 1-3 per million, most commonly in the age range 16-35 years and affecting males and females equally in most populations. There is no consistent human leucocyte antigen (HLA) association. Common features are the high, spiking pyrexia, arthralgia or arthritis, and a characteristic rash.

### Clinical features

The fever typically appears in the evening. Spikes in excess of 39 °C are typical, though a return to a normal temperature does not occur in 20% of cases. Arthralgia is almost universal and can intensify during the febrile episodes. Distal interphalangeal joint involvement, seen in one in five patients, is useful to distinguish it from other inflammatory arthropathies. The classic Still's rash is a maculopapular, salmon-pink rash on the trunk, thighs and arms or axillae, which appears during the temperature spike. The rash can also appear on the face, palms and soles and at sites of skin trauma (the Koebner phenomenon) in a third of adults. A severe sore throat (culture-negative) is relatively common in adults.

Other common manifestations are hepatosplenomegaly, with or without generalised lymphadenopathy, and polyserositis, of which pericarditis (in a third of cases) and pleuritis are the most common. Rare features include sicca symptoms (dry eyes, mouth), myocarditis, restrictive lung disease, liver or renal failure, panophthalmitis or inflammatory orbital pseudotumour, epilepsy, intravascular coagulopathy or haemophagocytic syndrome, and amyloidosis.

A 31-year-old woman presents for review. She complains of severe pain and restriction of movement affecting her right elbow, which is particularly bad on the outside of the arm. There is no past medical history of note and she is a keen gardener. The pain is reproduced on resisted wrist extension when the examiner fixes the right elbow.

Which one of the following diagnoses fits best with this clinical history?

A	Medial epicondylitis
B	Lateral epicondylitis
C	Cervical radiculopathy
D	Osteoarthritis of the elbow
E	Medial collateral ligament instability



# Explanation

## Tennis elbow

Lateral epicondylitis (so-called tennis elbow) is caused by inflammation of the musculotendinous origin of the common extensors on the lateral side of the elbow. It is most prevalent in the 20-40-year age group and is seen in up to 10-15% of regular tennis players.

On examination there is local tenderness over the lateral epicondyle and resistance against wrist extension reproduces the pain. Management involves rest, ice after exercise, stretching physiotherapy exercises, non-steroidal anti-inflammatory drugs and local steroid injections. A counterforce brace may be useful and patients resistant to conservative therapy may be referred for surgery to effect a lateral release.

A 60-year-old woman complains of feelings of aching and heaviness in both legs on walking that causes her to stop walking and bend or sit down. Extending the back aggravates the symptoms. An X-ray of the spine is normal.

What is the most likely diagnosis?

- |   |  |
|---|--|
| A | Lumbar disc prolapse                                       |
| B | Lumbar spondylolisthesis                                   |
| C | Spinal stenosis  |
| D | Osteoarthritis of the lumbar vertebrae                     |
| E | Crush fracture of the lumbar vertebrae due to osteoporosis |



# Explanation

## Spinal stenosis

This patient has spinal stenosis. Reduction in spinal canal diameter usually due to osteoarthritis may cause spinal claudication while walking. Root compression symptoms may occur. The straight leg-raising test is negative in spinal stenosis.

## Differential diagnosis

- + Restricted forward flexion with pain radiating into the buttocks or down the legs (sciatica) characterises lumbar disc prolapse. Extension of the back usually relieves the symptoms.
- + Displacement (usually forward) of one lumbar vertebra upon another is seen in spondylolisthesis. The X-ray picture is diagnostic.
- + Osteophytes might be seen in the intervertebral joints in osteoarthritis and the disc space might be narrowed.
- + Vertebral fracture due to osteoporosis would be evident on X-ray.

A 30-year-old woman presents with severe scaly, erythematous lesions all over her body. She has also developed swelling and severe pain in her distal interphalangeal joints.

Given the diagnosis of psoriasis, what treatment is likely to be most suitable for her?

A	Topical corticosteroids
B	Diclofenac
C	Coal tar
D	Long-wave ultraviolet radiation (psoralen ultraviolet A; PUVA)
E	Methotrexate

## Explanation

### Treatment of severe psoriasis and arthropathy

This is a potentially disabling severe form of psoriasis that justifies the use of methotrexate. This drug may interact with co-trimoxazole and non-steroidal anti-inflammatory drugs (NSAIDs). A liver biopsy may be indicated yearly to detect the cirrhosis that may occur in 5% of users. The full blood count needs to be monitored. Topical corticosteroids, coal tar and PUVA may reduce the skin lesions but will have no effect on psoriatic arthritis.

A 39-year-old man with coeliac disease presents complaining of pain in both legs and difficulty walking. An X-ray shows linear areas of low density surrounded by sclerotic borders in both femurs.

Given the most likely explanation for his lower-limb symptoms, which blood test would be most useful in diagnosing this condition?

A	Plasma calcium
B	Parathyroid hormone level
C	Serum phosphate
D	Serum alkaline phosphatase
E	Urinary phosphate excretion



# Explanation

## Investigations in osteomalacia

The history and results of the investigations suggest that this patient has developed osteomalacia, which can occur due to malabsorption of vitamin D in patients with coeliac disease. Blood results will show:

- + The plasma calcium concentration is low or normal
- + Parathyroid hormone can be elevated if there is secondary hyperparathyroidism
- + The serum phosphate level might be low due to increased parathyroid hormone-dependent phosphaturia, though this is variable
- + Serum 25-hydroxycholecalciferol is usually low (except in vitamin D-resistant rickets)
- + Alkaline phosphatase is reliably elevated in osteomalacia, for this reason it is the preferred answer here

A 55-year-old man complains of a gritty sensation in his eyes, red spots on both calves and pain in his wrists and hands. Titres of anti-Ro (SS-A) and anti-La (SS-B) are high.

What is the most likely diagnosis?

A	Systemic lupus erythematosus
B	Sjögren's syndrome
C	Avitaminosis A
D	Stevens-Johnson syndrome
E	Sarcoidosis



# Associated eye conditions in rheumatic diseases

- + Sjögren syndrome is associated with keratoconjunctivitis sicca and/or xerostomia. Dysphagia, neuropathy, renal involvement, otitis media and hepatosplenomegaly are common. Anti-Ro (SS-A) and anti-La (SS-B) titres are high and are characteristic for Sjögren syndrome.
- + Systemic lupus erythematosus (SLE) is a non-organ-specific autoimmune disease that is nine times more common in women. The age of onset is usually 15-25 years. Conjunctivitis can occur in SLE.
- + Stevens-Johnson syndrome usually occurs in response to a drug (sulphonamides, penicillins) a viral or other infection (orf, herpes simplex), neoplasia or systemic disease. The patient can be systemically very ill, with fever, arthralgia, myalgia, pneumonitis and/or uveitis. Vesicles develop in the mouth, genitourinary tract and/or conjunctiva. Target lesions of erythema multiforme may be seen on the skin.
- + Sarcoidosis presents classically as bilateral hilar lymphadenopathy on chest X-ray. In a third of cases this presents with cough, fever, arthralgia, malaise or erythema nodosum. These are painful erythematous nodular lesions on the anterior aspect of the shins. Anterior or posterior uveitis may also occur in this condition.

Xerophthalmia and keratomalacia are manifestations of vitamin A deficiency. The peak incidence is 2-5 years of age. Other features such as arthritis and purpuric spots are not seen.

A 47-year-old shopkeeper who has been on analgesics for rheumatoid arthritis for the past 2 years now complains of increasing pain, stiffness and swelling in his finger joints.

Which radiological feature would be most suggestive of rheumatoid arthritis?

A Subchondral sclerosis

B Decreased joint space

C Periarticular osteoporosis

D Lipping at the joint margins

E Punched out, lytic lesions in juxta-articular bone

## Explanation

### Radiographic signs in arthritides

- + Periarticular osteoporosis is a characteristic X-ray finding in patients with rheumatoid arthritis.
- + Subchondral sclerosis and lipping at the joint margins are characteristic features of osteoarthritis.
- + Decreased joint space occurs in both rheumatoid arthritis and osteoarthritis.
- + Punched out, lytic lesions in juxta-articular bone are seen in gouty arthritis.



A 38-year-old man presents with progressive breathlessness, dry cough and difficulty in swallowing. He also notes that his hands become pale and painful when exposed to the cold and that his fingers are swollen and stiff. His blood pressure is 160/110 mmHg. Chest radiographs show patchy shadows in both mid-zones and bases.

What diagnosis could best explain these findings?

A	Sarcoidosis
B	Limited cutaneous scleroderma
C	Diffuse cutaneous scleroderma
D	Rheumatoid arthritis
E	Sjögren's syndrome

# Explanation

## Systemic causes of dysphagia

Diffuse cutaneous scleroderma commences with swelling and stiffness of the fingers and is followed by extensive sclerosis. Heartburn, reflux or dysphagia is almost invariable.

Raynaud's phenomenon usually starts just before or with the onset of the disease, in contrast to limited cutaneous scleroderma, in which Raynaud's phenomenon precedes the disease by many years. Renal involvement can be acute or chronic and can lead to hypertension. Lung disease, both fibrosis and pulmonary hypertension, contribute significantly to mortality.

Sjögren syndrome is associated with keratoconjunctivitis sicca and/or xerostomia. Dysphagia, neuropathy, renal involvement, otitis media and hepatosplenomegaly are common. The lungs are not usually involved.

Sarcoidosis presents classically as bilateral hilar lymphadenopathy on chest X-ray. It is asymptomatic in one-third of patients. Dysphagia is not usually a feature. Raynaud's phenomenon is not a feature of rheumatoid arthritis.



A 30-year-old woman presents with fever, muscle and joint pains and fatigue. Erythema in a butterfly distribution is seen on her cheeks and across the bridge of her nose.

What is the most common finding that you would expect to see on investigation of her joints?

A Thickening of joint capsule

B Tendon contraction

C Soft tissue swelling

D Aseptic necrosis

E Bony erosions

## Explanation

### Joint X-ray appearances in SLE

This patient has features suggestive of systemic lupus erythematosus (SLE). Joint involvement is the most common clinical feature (> 90%). The joints may appear clinically normal, although sometimes there is soft-tissue swelling surrounding the joint. Deformity because of joint capsule and tendon contraction is rare, as are bony erosions. Aseptic necrosis affecting the hip or knee is a rare complication of the disease.

A 65-year-old woman complains of increased morning stiffness, particularly in her shoulder girdle, so that she can't get up and has to roll out of bed. The stiffness lasts approximately 2 hours. She also complains of fatigue and of being depressed.

What is the most likely diagnosis?

A Systemic lupus erythematosus

B Osteoarthritis

C Rheumatoid arthritis

D Polymyalgia rheumatica

E Sjögren's syndrome



# Explanation

## Polymyalgia rheumatica

Although the most common age group involved is that between 60 and 70 years, a third of patients with polymyalgia rheumatica are aged under 60 years. Initial symptoms are seldom seen before 45 years or after 80 years of age. The male to female ratio is 1:2. The onset is often dramatic, with some patients giving the precise date of their first symptoms, and in most cases it is fully developed within a month.

### Clinical features

Pain and stiffness are usually localised to muscles, although tenderness is not as severe as in myositis. There can be additional tenderness involving periarticular structures. The onset is most common in the shoulder girdle, spreading to involve both shoulders, the pelvic girdle and proximal muscles with striking symmetry. Involvement of distal muscles is unusual. Immobility is most severe on waking; a characteristic complaint is the need to roll out of bed, often with the aid of a partner. This morning stiffness can persist for hours.

Most patients look unwell and complain of general malaise, fatigue and depression. Anorexia and weight loss can be striking, often suggesting neoplasia, while night sweats and fever are frequent and are occasionally the presenting feature.

### Diagnosis

Diagnosis is usually made on the presence of a symptomatic response to steroid therapy and raised inflammatory markers, in the absence of other significant underlying pathology. Arterial biopsy may confirm the presence of giant cell arteritis, although a negative biopsy doesn't exclude the diagnosis.



A 52-year-old woman with a long history of rheumatoid arthritis comes to the Emergency Department with bilateral, painful red eyes which have become increasingly uncomfortable over the past few days. There is watering and photophobia, and she tells you the pain has been particularly bad on the night prior to coming to the department. Scleral, episcleral and conjunctival vessels all appear engorged, there appears to be scleral thinning and some yellow necrotic areas present in both sclerae.

Which of the following would be considered a complication of this woman's eye disease?

A	Cataract formation
B	Macular hole formation
C	Retinal artery occlusion
D	Retinal haemorrhage
E	Retinal vein occlusion

## Explanation

The answer is Cataract formation -

The history and examination here is suggestive of an underlying diagnosis of scleritis, with the yellow necrotic areas suggestive of scleromalacia. Scleritis is associated with a number of longer term ocular complications. These include:

- + Keratopathy, leading to peripheral corneal thinning, acute stromal keratitis, sclerosing keratitis, or peripheral ulcerative keratitis
- + Uveitis, both anterior and posterior uveitis are seen
- + Glaucoma
- + Cataract
- + Fundus abnormalities including choroidal folds, disk edema, macular edema, annular ciliochoroidal detachment, or serous retinal detachment

You are reviewing a research proposal for a trial of a new tumour necrosis factor alpha (TNF- $\alpha$ ) antagonist.

When reviewing the profile of TNF- $\alpha$ , which of the following is true?

- |   |  |
|---|--|
| A | Raised levels lead to increased insulin resistance |
| B | Acts on only one target cell                       |
| C | The gene coding for it is found on chromosome 7    |
| D | TNF-alpha is produced only by macrophages          |
| E | Lipopolysaccharide inhibits TNF-alpha production   |



## Explanation

### Tumour necrosis factor alpha (TNF- $\alpha$ )

- + TNF is a 212-amino-acid protein, coded for by a gene on chromosome 6.
- + It is a neutrophil chemoattractant, stimulates macrophage phagocytosis and helps drive the acute-phase response.
- + Lipopolysaccharide exposure leads to increased TNF- $\alpha$  production.
- + Raised levels of TNF- $\alpha$  lead to increased insulin resistance, because TNF- $\alpha$  promotes phosphorylation of IRS-1 (insulin receptor substrate 1).
- + TNF- $\alpha$  acts on a range of targets, including the hypothalamus, liver, neutrophils and macrophages.
- + TNF- $\alpha$  antagonists have a role to play in the management of seronegative arthritides, Crohn's disease, psoriasis and rheumatoid arthritis.

A 20-year-old college student complains of increasing back pain and early morning stiffness. An X-ray of his lower back shows erosion of the apophyseal joints and obliteration of the sacroiliac junction.

Given the most likely clinical diagnosis from these findings, what treatment would be most suitable for him?

A	Oral NSAIDs
B	Colchicine
C	Intra-articular steroid injections
D	Spinal osteotomy
E	Bedrest and immobilisation

## Explanation

### Management of ankylosing spondylitis

Ibuprofen is the preferred analgesic for back pain in ankylosing spondylitis. Patients with ankylosing spondylitis should be encouraged to remain active and follow their normal pursuits as far as possible. Spinal extension exercises and regular physiotherapy are most useful.

Spinal osteotomy is rarely used to correct deforming kyphosis. Rest and immobilisation are contraindicated as they may lead to muscle wasting, osteoporosis and ankylosis. Intra-articular steroid injections are not helpful.



A 24-year-old man comes to the Rheumatology Clinic with severe back pain, particularly during the mornings. He also has symptoms of ulcerative colitis for which are treated with steroid enemas. He is treated with Naproxen for his back pain, but with additional regular Paracetamol this is still not controlling it. He has a diagnosis of ankylosing spondylitis. On examination he has reduced chest expansion and limited forward and lateral flexion because of stiffness.

Investigations;

Hb	13.3 g/dl
WCC	$7.1 \times 10^9/l$
PLT	$189 \times 10^9/l$
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	110 micromol/l
ESR	67 mm/1 <sup>st</sup> hour

Which of the following is the most appropriate next step?

A Add Azathioprine

B

Add Etanercept

C

Add Methotrexate

D

Add Prednisolone

E

Switch Naproxen to Diclofenac

## Explanation

The answer is Switch Naproxen to Diclofenac

This man has uncontrolled symptoms of AS, the appropriate treatment pathway is a trial of an alternative NSAID, then moving on to an anti-TNF biological if symptoms are still not controlled according to NICE guidance. Etanercept, Golimumab and Adalimumab are all potential options. In contrast to other inflammatory arthritides, steroids and steroid sparing agents are not a part of the recommended therapeutic cascade. Consideration of risk TB is recommended prior to starting anti-TNF therapy.



A 28-year-old man presents to the clinic with painful knees and ankles. He is noted to have a rash on the glans penis. He has a history of urethritis due to *Chlamydia trachomatis*. He has also recently attended the Ophthalmology Department for an episode of uveitis.

What is the most likely diagnosis?

A	Reactive arthritis
B	SLE
C	Gouty arthritis
D	Septic arthritis
E	Rheumatoid arthritis

# Explanation

## Reactive arthritis

The classic triad of arthritis, urethritis and conjunctivitis was previously known as Reiter syndrome, but is now referred to as reactive arthritis. It often occurs with mucocutaneous lesions. Uveitis or episcleritis may also occur as ocular findings. A similar spectrum of clinical manifestations can be triggered by enteric infection with any of several *Shigella*, *Salmonella*, *Yersinia* and *Campylobacter* species and by genital infection with *Chlamydia trachomatis* (an organism particularly associated with reactive arthritis). Reactive arthritis has a strong HLA-B27 association and is a seronegative spondyloarthropathy. The arthritis is usually asymmetrical and additive. There is no sepsis and joint aspirates are sterile.

The history and findings here are not suggestive of rheumatoid arthritis.

A 55-year-old woman with a history of systemic lupus erythematosus complains of loss of vision. On examination she is found to have multiple opacities in the lenses of both eyes.

What is the most appropriate treatment in this case?

- |   |                               |
|---|-------------------------------|
| A | Intraocular steroids          |
| B | Laser treatment               |
| C | Vitrectomy                    |
| D | Extracapsular lens extraction |
| E | Timolol                       |



## Explanation

### Cataract in SLE

Systemic lupus erythematosus (SLE) is a non-organ-specific autoimmune disease characterised by antinuclear antibodies and vasculitis. Women are most commonly affected. Cataracts may occur earlier than normal in this condition. The treatment is surgical removal of the lens. Extracapsular extraction with a posterior-chamber lens implant is the usual treatment of choice.

A 31-year-old woman recently arrived in the UK from Somalia complains of marked neck pain, with pins and needles affecting the left arm associated with poor grip strength of the left hand. Examination reveals her to be tender over the cervical spine with spasm of trapezius on the left hand side.

Radiographs of the cervical spine show narrowing of the C3/4 and C4/5 joint spaces and partial collapse of C4. Investigations show: haemoglobin 9.8 g/dl, white cell count (WCC)  $11.8 \times 10^9/l$ , lymphocytes  $9.2 \times 10^9/l$ , platelets  $567 \times 10^9/l$ , erythrocyte sedimentation rate (ESR) 121 mm in 1st hour, C-reactive protein (CRP) 256 mg/l, calcium 2.15 mmol/l, albumin 35 g/l, alkaline phosphatase 185 U/l, phosphate 0.9 mmol/l.

What is the most likely diagnosis?

A	Multiple myeloma
B	Pott's disease
C	Osteoporotic collapse
D	Disseminated malignancy
E	Osteomalacia

## Explanation

### Pott's disease

Pott's disease is the most likely diagnosis owing to the marked acute-phase response with a lymphocytosis in an ethnic group at increased risk of tuberculosis (TB). It may manifest in spondylitis (especially of the lower thoracic spine), paraspinous TB abscesses, psoas abscess or cord compression. The elevated alkaline phosphatase in this case is caused by the recent fracture rather than by metabolic bone disease. Although standard anti-TB therapy for pulmonary TB lasts for 6 months, treatment for a 12-month period is recommended for patients with TB of the bone.



A 69-year-old diabetic woman is febrile with chills and rigors and has a 1-day history of pain in her right knee.

What clinical diagnosis should be considered most likely until excluded?

A Gouty arthritis

B Osteoarthritis

C Pseudogout

D Septic arthritis

E Reactive arthritis

## Explanation

### Septic arthritis

This woman has septic arthritis. Involvement of a single joint occurs in 90% of cases. The knee is most commonly affected.

Gout is more likely to affect the first metatarsophalangeal joint and is also not associated with fever, chills and rigors. Osteoarthritis is a degenerative process and does not present as an acute condition. Pseudogout is the deposition of calcium pyrophosphate crystals in a joint that is already affected by arthritis. These patients usually have long-standing pain and several joints may be involved. Reactive arthritis is commonly seen in younger people, with a preponderance in men, occurring 4-6 weeks after a genitourinary or gastrointestinal infection.

You review a 54-year-old woman who has long-standing rheumatoid arthritis. Which one of the following are common features of rheumatoid arthritis?

- |   |   |
|---|---|
| A | Ulcerative colitis                                      |
| B | Uveitis   |
| C | Proteinuria from renal deposition of amyloid            |
| D | A monarticular picture                                  |
| E | Proximal interphalangeal joint involvement in the hands |



# Explanation

## Features associated with rheumatoid arthritis

- + Rheumatoid arthritis commonly presents with a polyarticular picture, the metacarpophalangeal and the proximal interphalangeal joints are the usual sites of involvement in the hands.
- + Scleritis and episcleritis are more common ocular manifestations of rheumatoid arthritis than uveitis and are usually managed with local and/or systemic corticosteroids.
- + Disease-modifying agents used for treating rheumatoid arthritis are a more common cause of proteinuria in rheumatoid arthritis than amyloid deposition.

Ulcerative colitis and inflammatory bowel disease are associated with seronegative arthritides, not rheumatoid arthritis.

A 62-year-old woman presents for review. She has suffered from joint pains and arthritis for the past few years. Blood testing reveals positive rheumatoid factor.

What is the most common human leucocyte antigen (HLA) type in rheumatoid arthritis?

A	HLA B5
B	HLA B27
C	HLA DR2
D	HLA DR3
E	HLA DR4

# Explanation

## HLA type and rheumatoid arthritis

Of the human leucocyte antigen (HLA) types, HLA DR4 is associated with increased development of rheumatoid arthritis, vitiligo, pemphigus vulgaris and diabetes mellitus. Class II antigens (the HLA-D series) are expressed on antigen-presenting cells (B cells, monocytes/macrophages, Langerhans cells, dendritic cells and activated T cells). Rheumatoid arthritis is typified by widespread persistent synovitis.

The development of synovitis is thought to be related to the local production of rheumatoid factors and cytokines by plasma cells. Activated lymphocytes and macrophages in the synovium add to the rich mix of cytokines, producing interleukins, prostaglandins and tumour necrosis factor alpha.

HLA DR3 is associated with diabetes mellitus, and DR2 appears protective against autoimmune diseases. B27 is associated with seronegative arthritis and inflammatory bowel disease. HLA B5 is associated with increased risk of Behcet's.



An 8-year-old boy presents with a 6-month history of gradually progressive swelling and pain below the right knee. On examination, the knee joint appears normal. An X-ray shows a lytic lesion with sclerotic margins in the upper tibial metaphysis.

What is the most probable diagnosis?

A	Osteogenic sarcoma
B	Brodie's abscess
C	Classical osteomyelitis
D	Osteoclastoma
E	Ewing's sarcoma

## Leg pain and swelling in a child

- + Brodie's abscess (the correct answer here) is a form of chronic osteomyelitis that arises insidiously. A localised abscess is present within the bone, often near the site of the metaphysis. Deep 'boring' pain is often the predominant symptom. The X-ray is usually characteristic.
- + In patients with osteogenic sarcoma the X-ray typically shows a raised periosteum (Codman's triangle) with evidence of new bone formation under the corners, and a 'sun-ray' appearance caused by well-marked radiating spicules of new bone within the tumour.
- + Chronic osteomyelitis is nearly always a sequel to acute osteomyelitis. The bone is thickened and generally denser than normal. Sequestra are commonly present within cavities in the bone. There might be a sinus track leading to the skin surface discharging pus. X-rays show thickened bone with irregular and patchy sclerosis that gives a honeycombed appearance. Sequestra are seen as dense loose fragments lying within a cavity in the bone.
- + Osteoclastoma occurs most commonly in young adults aged 20-40 years. The X-ray shows a soap-bubble appearance with no or minimal sclerosis.
- + Ewing's sarcoma is a highly malignant tumour that arises in bone marrow. The tumour is therefore common in the shafts of the femur, tibia or humerus. It arises in the diaphysis rather than the metaphysis of the bone. Radiographs show destruction of bone and concentric layers of subperiosteal new bone (an 'onion peel' appearance).

A young African-American woman is diagnosed as having systemic lupus erythematosus. What is the characteristic epidemiological feature of this condition?

- A It is about twice as common in women than in men
- B The highest incidence is amongst Caucasian women
- C The age of onset is usually over 40 years
- D It is associated with HLA-B8 and -DR3 in Caucasians
- E First-degree relatives have a 25% chance of developing the disease



- |   |  |
|---|--|
| A | It is about twice as common in women than in men                   |
| B | The highest incidence is amongst Caucasian women                   |
| C | The age of onset is usually over 40 years                          |
| D | It is associated with HLA-B8 and -DR3 in Caucasians                |
| E | First-degree relatives have a 25% chance of developing the disease |

## Explanation

### Epidemiology of SLE

- + Systemic lupus erythematosus (SLE) is most common in African-American women, with a prevalence of 1:250.
- + It is about nine times as common in women than in men.
- + It has a peak age of onset between 20 and 40 years.
- + There is an increased frequency of HLA B8 and HLA DR3 in white Europeans.
- + First-degree relatives have a 3% chance of developing the disease.
- + There is a higher concordance rate in monozygotic twins (up to 25%).



A 62-year-old woman comes to the Rheumatology Clinic with severe rheumatoid arthritis. She is currently taking a second-line agent, low-dose prednisolone and a non-steroidal anti-inflammatory drug. Despite this she still has active disease and wants to increase her therapy if possible. You are considering using etanercept, an anti-tumour necrosis factor (anti-TNF) agent in this patient.

Which one of the following interactions or previous illnesses would prompt caution or avoidance of etanercept?

A	Use in a patient with previous hepatitis B, no residual hepatitis / virus identified
B	Use in conjunction with sulphasalazine
C	Use in conjunction with methotrexate
D	Use in a patient with previous iron deficiency anaemia
E	Use in a patient with previous history of psoriasis

A	Use in a patient with previous hepatitis B, no residual hepatitis / virus identified
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E	Use in a patient with previous history of psoriasis

## Explanation

### Etanercept

Studies of etanercept in combination with sulfasalazine demonstrated a statistically significant reduction in the white blood cell count. This should prompt caution when the two are used in combination. Other cautions include its use in patients with active hepatitis B or hepatitis C or with multiple sclerosis. The caution which everyone is aware of with anti-tumour necrosis factor (TNF) agents is, of course, the risk of reactivation of tuberculosis in patients who have a previous history of the disease.

A 40-year-old woman presents with a 5-year history of Raynaud's phenomenon. She now complains being unable to extend her fingers and has developed a painful ulcer on the tip of her right index finger.

Which antibodies are most likely to be present in this condition?

A	Anti smooth muscle antibodies
B	Anticentromere antibodies
C	Anti-topoisomerase-1 antibodies
D	Anti-RNA polymerase antibodies
E	Anti-Ro (SSA) antibodies



A	Anti smooth muscle antibodies
B	<b>Anticentromere antibodies</b>
C	Anti-topoisomerase-1 antibodies
D	Anti-RNA polymerase antibodies
E	Anti-Ro (SSA) antibodies

## Explanation

### Antibodies in rheumatic diseases

- + The features are suggestive of limited cutaneous scleroderma, which occurs in 60% of people with systemic sclerosis. Speckled, nucleolar or anticentromere antibodies occur in 70-80% of patients.
- + Anti-topoisomerase-1 and anti-RNA polymerase antibodies are seen in 25-30% of people with diffuse cutaneous scleroderma.
- + Antinuclear antibodies are non-specific for this disease, while anti-Ro antibodies are characteristic of Sjögren syndrome.



A 62-year-old woman is being treated for a pathological fracture of her right femur. An X-ray of the femur shows patchy sclerosis, thickening of the trabeculae and dedifferentiation.

Given the likely diagnosis, what treatment would be most appropriate for her?

A	Calcium supplements
B	Calcitonin
C	Hormone replacement therapy
D	Tiludronate
E	Raloxifene

A	Calcium supplements
B	Calcitonin
C	Hormone replacement therapy
D	Tiludronate
E	Raloxifene

## Explanation

### Treatment of Paget's disease

This woman has Paget's disease. Bisphosphonates are the mainstay of treatment. These analogues of normal bone pyrophosphate adhere to hydroxyapatite and inhibit osteoclasts. New bone formed after treatment is lamellar and not woven. This reflects a normalisation of bone turnover rather than a direct effect on osteoclasts. Tiludronate is an oral bisphosphonate.

Calcium supplements, calcitonin, hormone replacement therapy and raloxifene would be useful if she had postmenopausal osteoporosis.

A 44-year-old man presents with fatigue, low-grade fever and weakness. Because of muscle weakness, he can no longer climb the stairs to his first-floor flat. Over the past few weeks, a violaceous rash has appeared on his cheeks.

What is the most probable diagnosis?

A	Dermatomyositis
B	Chronic fatigue syndrome
C	Polymyalgia rheumatica
D	Multiple sclerosis
E	Guillain-Barré syndrome

# Explanation

## Dermatomyositis

Symmetrical proximal muscle weakness resulting from muscle inflammation is seen in polymyositis. In around 25% of cases patients have a purple (heliotrope) rash) on the cheeks, eyelids and light-exposed areas (dermatomyositis).

### Differential diagnosis

- + Polymyalgia rheumatica is common in older women and presents as aching and morning stiffness in the proximal muscles.
- + Multiple sclerosis may present with unilateral optic neuritis, progressive weakness of the legs or many other neurological symptoms. Low-grade fever is not a feature of multiple sclerosis.
- + Guillain-Barré syndrome (acute postinfective polyneuritis) presents with back and limb pain, followed by progressive ascending paralysis. The proximal muscles may be more affected and deep tendon reflexes are absent. Skin lesions do not occur.
- + Fibromyalgia presents with fatigue and weakness but is not usually restricted to the lower limbs. Pain is the chief symptom in this condition for which no cause can be found. Muscle tenderness is not confined to the areas of weakness but is diffuse.



A 73-year-old man presents with malaise, anorexia, pain in his shoulders and hips and a weight loss of 8.7 kg that have developed over the past 3 months. Examination is unremarkable, except for mildly painful limitation of movement of his hips and shoulders. His ESR is elevated at 72. CK is in the normal range.

What is the most likely diagnosis?

A	Polymyositis
B	Systemic lupus erythematosus
C	Rheumatoid arthritis
D	Polymyalgia rheumatica
E	Gout

## Explanation

### Polymyalgia rheumatica

People with polymyalgia rheumatica have a raised erythrocyte sedimentation rate (ESR) and are at increased risk of cerebrovascular events, and should be treated with prednisolone. Systemic symptoms of PMR do include weight loss and anorexia. Polymyositis is associated with a rise in CK. SLE and rheumatoid arthritis are associated with symmetrical small joint polyarthrititis, and SLE in particular with the typical facial rash. Gout is usually associated with monoarthrititis.

A 42-year-old woman presents to the Rheumatology Clinic for review. Over the past 2 months she has suffered increasing pain, tingling and numbness in the early hours of the morning over the thumb, index and middle fingers of the right hand. She has recently been diagnosed with Type 2 diabetes which is managed with diet and exercise only. She puts her symptoms down to lifting two young children who are three and five years old. On examination her BP is 145/85 mmHg; pulse is 80/min and regular. Her BMI is 31. Phalen's test is positive on examination of the right hand.

Which of the following is the most appropriate intervention?

A	Local corticosteroid injection
B	Low dose oral corticosteroids
C	Regular Naproxen
D	Splinting
E	Surgical release

A	Local corticosteroid injection
B	Low dose oral corticosteroids
C	Regular Naproxen
D	Splinting
E	Surgical release

## Explanation

The answer is Local corticosteroid injection -

In this situation splinting is not a realistic option for treatment of carpal tunnel syndrome. With regards to local corticosteroid injection, up to 70% of patients show a symptom response within 1 month. There is no evidence that NSAIDs are of value in treating the condition, and low dose oral corticosteroids do not have a positive benefit risk profile in this situation. In the event that the response to local corticosteroids is insufficient, progression to surgery is appropriate.



A 55-year-old obese patient complains of a 4-month history of moderate pain in her finger joints, mainly at the end of the day, which improves with rest. She has also noticed some swelling. On examination there is tenderness to palpation and enlargement of the distal interphalangeal joints.

What is the most likely diagnosis?

A	Rheumatoid arthritis
B	Systemic sclerosis
C	Osteoarthritis
D	Fibromyalgia
E	Gout

# Osteoarthritis

## Pain in osteoarthritis

Pain is the predominant symptom of osteoarthritis, usually mild to moderate in nature and it increases with joint use and at the end of the day. Pain is generally improved with rest and moderation of activity. Severe disease can cause pain at rest or at night. The source of pain can be underlying bone, the joint capsule or surrounding structures. Cartilage is avascular and without nerves and not itself a source of pain.

## Examination

Physical examination reveals tenderness to palpation, bony thickening (osteophyte formation), small effusions and crepitus. Specific joint findings also occur:

- + Typical findings in the hand are bony enlargement of the proximal interphalangeal joints (Bouchard's nodes) and the distal interphalangeal joints (Heberden's nodes). The first carpometacarpal joint may be involved, causing a squared appearance of the lateral aspect of the hand.
- + Involvement of the foot leads to bunions.
- + In the knee there can be pronounced valgus and varus deformities, Baker's cyst or locking (suggesting meniscal damage).
- + Early hip findings include limited internal and external rotation.
- + Back findings include pain; true osteoarthritis occurs at the apophyseal joints; degenerative disc disease and diffuse idiopathic skeletal hyperostosis are distinct entities.

A 27-year-old woman known to suffer from epilepsy has been admitted with a history of dizzy spells and a swollen left calf. Her blood pressure recordings confirm a postural drop in her systolic reading of over 20 mmHg. Her biochemistry shows a sodium concentration of 126 mmol/l and a potassium concentration of 6.1 mmol/l. Her blood count is normal apart from a low platelet count. She has no past history of any surgical procedure but has a history of three spontaneous miscarriages. The nurse has noticed that at times she makes jerky explosive movements of her limbs.

What is the underlying diagnosis?

- |   |   |
|---|---|
| A | Uncontrolled epilepsy                           |
| B | Idiopathic thrombocytopenic purpura             |
| C | Antiphospholipid syndrome                       |
| D | Syndrome of inappropriate ADH (SIADH) secretion |
| E | Dehydration                                     |



A	Uncontrolled epilepsy
B	Idiopathic thrombocytopenic purpura
C	Antiphospholipid syndrome
D	Syndrome of inappropriate ADH (SIADH) secretion
E	Dehydration

## Explanation

### Antiphospholipid syndrome

Antiphospholipid syndrome is characterised by the presence of antiphospholipid antibodies, which cause thrombosis through an effect on platelet membranes, endothelial cells and on prothrombin, protein C and protein S. It is characterised by recurrent abortions, epilepsy, chorea, migraine and Addison's disease. The low sodium and elevated potassium seen here raises the possibility of adrenal involvement leading to Addison's.



A 55-year-old man presents arthralgia affecting his hands, wrists, elbows and knees. He has been living and working in Portugal, where he runs a hotel and bar. Past medical history of note includes erectile dysfunction, which is managed with sildenafil. He has no children and no partner at the current time. On examination he looks tanned, his blood pressure is 139/72 mmHg and his body mass index (BMI) is 27 kg/m<sup>2</sup>. Investigations show: haemoglobin 11.0 g/dl, white cell count  $8.7 \times 10^9/l$ , platelets  $181 \times 10^9/l$ , sodium 139 mmol/l, potassium 4.4 mmol/l, creatinine 110  $\mu\text{mol/l}$ , alanine aminotransferase (ALT) 132 U/l, alkaline phosphatase 160 U/l, bilirubin 76  $\mu\text{mol/l}$ , fasting blood glucose 9.1 mmol/l.

Which one of the following is the most likely diagnosis?

A	Type 2 diabetes
B	Wilson's disease
C	Pseudogout
D	SLE
E	Haemochromatosis

A	Type 2 diabetes
B	Wilson's disease
C	Pseudogout
D	SLE
E	Haemochromatosis

## Explanation

### Haemochromatosis

This patient has evidence of hepatic dysfunction, diabetes, joint pains and increased skin pigmentation; this picture is entirely in keeping with a diagnosis of haemochromatosis. Excess iron deposition in the pancreas leads to  $\beta$ -cell failure and diabetes mellitus; iron deposition in the liver leads to cirrhosis; and pituitary iron deposition leads to hypogonadism. The gene responsible for the development of the disease is named *HFE* and is found on chromosome 6. Regular phlebotomy to reduce total body iron stores is the treatment of choice.

A 26-year-old man who is being treated for chlamydial urethritis complains of pain and swelling in his left ankle, pain in the soles of his feet, a rash on the palms of both hands and gritty, red eyes.

What could the diagnosis be?

- |   |                       |
|---|-----------------------|
| A | Behçet's disease      |
| B | Reactive arthritis    |
| C | Felty syndrome        |
| D | Psoriatic arthropathy |
| E | Gonococcal arthritis  |



## Explanation

### Reactive arthritis (formerly Reiter syndrome)

This patient has reactive arthritis. Urethritis, conjunctivitis, reactive arthritis, plantar fasciitis and keratoderma blennorrhagica (a rash on the palms and soles) are suggestive of this syndrome. It is predominantly a disease of young men, with a male to female ratio of 15:1. The arthritis is of the reactive type, occurring after bacterial dysentery caused by *Salmonella*, *Shigella*, *Campylobacter* or *Yersinia* spp. or sexually acquired infection with *Chlamydia* spp. Joint aspiration shows the presence of giant macrophages (Reiter's cells).

### Differential diagnosis of arthralgia

Behçet's disease is a vasculitis of unknown aetiology that characteristically targets venules. Oral ulcers are common.

Felty syndrome is the association of splenomegaly and neutropenia with rheumatoid arthritis.

Psoriatic arthropathy affects the distal interphalangeal joints and is almost invariably associated with nail dystrophy.

In younger, sexually active patients, disseminated gonococcal infection is an important cause of arthralgia, which occurs in up to 3% of people with untreated gonorrhoea. This presents with migratory arthralgia, low-grade fever and tenosynovitis. Painful pustular skin lesions can also be present.

An elderly man complains of an acutely swollen left knee. An X-ray shows intra-articular calcification. Joint aspiration reveals small, rhomboid-shaped crystals.

These signs occur in which of the following?

- |   |                         |
|---|-------------------------|
| A | Acute gouty arthritis   |
| B | Osteoarthritis          |
| C | Rheumatoid arthritis    |
| D | Reactive arthritis      |
| E | Pyrophosphate arthritis |

A	Acute gouty arthritis
B	Osteoarthritis
C	Rheumatoid arthritis
D	Reactive arthritis
E	Pyrophosphate arthritis

## Explanation

### Pseudogout

Pseudogout (pyrophosphate arthritis) occurs as a result of the deposition of calcium pyrophosphate dihydrate crystals (chondrocalcinosis) in the large joints, particularly the knees. Small, rhomboid-shaped crystals are characteristic of pseudogout. Apart from ageing, the strongest association is with osteoarthritis.

### Association with osteoarthritis

The changes in osteoarthritic cartilage that encourage calcium pyrophosphate crystal deposition are:

- + A reduction in the concentration of proteoglycan and other natural inhibitors of crystal formation, and
- + Increased extracellular pyrophosphate levels occurring as a result of upregulated chondrocyte metabolism.



A 42-year-old woman with chronic arthritis complains of grittiness in her eyes and a dry mouth. Investigations reveal a positive Schirmer's test. Rheumatoid factor is present, as are anti-Ro and anti-La antibodies.

What is the most probable diagnosis?

- |   |                              |
|---|------------------------------|
| A | Systemic lupus erythematosus |
| B | Felty syndrome               |
| C | Still's disease              |
| D | Sjögren syndrome             |
| E | Episcleritis                 |

# Explanation

## Sjögren syndrome

Sjögren syndrome is the association of a connective tissue disease (rheumatoid arthritis in 50% cases) with keratoconjunctivitis sicca. There is decreased lacrimation and salivation as a result of infiltration of secretory glands by lymphocytes and plasma cells.

### Investigations

Rheumatoid factor is always positive and anti-Ro and anti-La antibodies characterise the condition. Conjunctival dryness can be quantified by Schirmer's test, in which a strip of filter paper is placed under the lower lid and the distance along the paper that tears are absorbed is measured – a distance of less than 10 mm in 5 minutes is positive.

### Differential diagnosis

Felty syndrome is long-standing rheumatoid arthritis with splenomegaly, lymphadenopathy, pigmentation, skin ulcers and leukopenia.

Still's disease is subdivided into juvenile chronic arthritis and adult-onset Still's disease. For diagnosis of the adult form, the following should be present:

- + Daily fever of  $> 39^{\circ}\text{C}$
- + Arthralgia/arthritis
- + Rheumatoid factor and antinuclear antibody- (ANA-) - negative
- + (Plus) any two out of: leucocytosis  $> 15 \times 10^9/\text{l}$ , serositis (pleural or pericardial), hepatomegaly, splenomegaly and/or lymphadenopathy

A 65-year-old woman being treated for epilepsy presents with bone pain and muscle weakness. Blood tests show increased serum alkaline phosphatase, plasma calcium at the lower limit of the normal range, and low serum phosphate levels. An X-ray of the femur reveals linear areas of low density surrounded by sclerotic borders.

What is the most likely diagnosis?

A	Osteoporosis
B	Osteomalacia
C	Paget's disease
D	Osteosarcoma
E	Polymyalgia rheumatica



# Explanation

## Osteomalacia

Osteomalacia is the diagnosis in this case. Anticonvulsants such as phenytoin and phenobarbital can induce liver enzymes that lead to an increased breakdown of 25-hydroxycholecalciferol, and this causes osteomalacia. The X-ray shows evidence of the Looser's zones, which are typical of osteomalacia.

## Differential diagnosis

- + In Paget's disease the serum alkaline phosphatase level will be raised but serum calcium and phosphate levels will be normal. The X-ray will also show a sclerotic phase of bone expansion, thickening of trabeculae and dedifferentiation (loss of distinction between cortex and trabeculae).
- + Blood tests are normal in people with osteoporosis. It is difficult to diagnose osteoporosis on the basis of X-rays, particularly of the long bones, as there are hardly any significant features.
- + In osteosarcoma the X-rays usually show irregular metaphyseal destruction, cortical erosion and new bone formation under a raised periosteum.

Polymyalgia rheumatica is not associated with any blood or X-ray abnormalities.

A 42-year-old man presents with an acutely swollen, painful right first metatarsophalangeal joint.

Which one of the following features would most reliably distinguish gout from septic arthritis as the cause?

A	A polymorph leukocytosis
B	Increased serum C-reactive protein
C	Hyperuricaemia
D	The presence of negatively birefringent crystals in synovial fluid
E	The presence of polymorph leucocytes in the synovial fluid

D	The presence of negatively birefringent crystals in synovial fluid
E	The presence of polymorph leucocytes in the synovial fluid

## Explanation

### Diagnosis of gout

A polymorph leucocytosis and increased serum C-reactive protein can occur in any acute inflammatory condition. Hyperuricaemia is frequently asymptomatic, and is not always present in clinical gout (especially when this has been precipitated by lowering of urate concentration, for example with allopurinol). Polymorphs are present in synovial fluid in gout, but the presence of monosodium urate crystals (which rotate the plane of polarised light) establishes the diagnosis.



A 35-year-old computer operator with rheumatoid arthritis comes to see you with an upper respiratory tract infection and malaise. He has a purpuric rash all over his body and, on examination, a mass is felt in the left upper quadrant of his abdomen. A full blood count shows: haemoglobin 7.3 g/dl, mean corpuscular volume (MCV) 79 fl, white cell count (WCC)  $2.5 \times 10^9/l$ , platelets  $47 \times 10^9/l$ .

What is the most probable diagnosis?

A	Fibrosing alveolitis
B	Rheumatoid pulmonary nodules
C	Caplan syndrome
D	Polyarteritis nodosa
E	Felty syndrome

## Explanation

### Extra-articular manifestations of rheumatoid arthritis

- + Felty syndrome is the association of long-standing (> 10 years) rheumatoid arthritis with splenomegaly, pancytopenia and recurrent infections. Weight loss, a vasculitic rash and ulceration can also occur.
- + Fibrosing alveolitis presents with progressive exertional dyspnoea and a dry, persistent cough. Chest expansion is poor and numerous bilateral end-inspiratory crepitations might be heard over the lower zones on auscultation.
- + Rheumatoid pulmonary nodules do not usually cause any symptoms.
- + The combination of rheumatoid nodules and pneumoconiosis is known as Caplan syndrome.

A purpuric rash might occur in polyarteritis nodosa but splenomegaly and pancytopenia do not.

A 51-year-old physical education instructor returns from a trekking expedition in the Far East complaining of pain and swelling in his left big and second toes. On examination the affected joints are red and swollen. Movement of the toes is painful.

What is the most probable diagnosis?

A	Acute gouty arthritis
B	Stress fracture
C	Osteoarthritis
D	Morton's metatarsalgia
E	Plantar fasciitis



A	Acute gouty arthritis
B	Stress fracture
C	Osteoarthritis
D	Morton's metatarsalgia
E	Plantar fasciitis

## Explanation

### Differential diagnosis of acute gouty arthritis

- + Excruciating pain, redness and swelling in the affected joint – often the metatarsophalangeal joint of the big toe – characterises acute gouty arthritis.
- + Stress (March) fractures occur in the shaft of the second or third metatarsal and may follow excessive walking.
- + Osteoarthritis is usually a degenerative disease of older age (> 55 years). Redness and swelling are not features of osteoarthritis.
- + Morton's metatarsalgia is pain due to pressure on an interdigital neuroma between the metatarsals. Pain usually radiates between the third and fourth clefts.
- + Plantar fasciitis may occur in certain arthritides and results in pain under the calcaneum (in the sole of the foot).

A 54-year-old man with a history of obesity, hypertension and Type 2 diabetes mellitus comes to the Emergency Department with an acutely painful, hot and red right knee, the movement of which is severely limited. He says this came up almost overnight, he was not exercising beforehand, and does not remember any cuts or scrapes. His diabetes is relatively well controlled on Metformin alone, (HbA1c 57 mmol/mol (7.4%)), and he has no microvascular complications from his diabetes. He is afebrile. His right knee is hot and swollen, with an obvious effusion, and the overlying skin is erythematous. Flexion is limited to only 20 degrees.

Which of the following is the diagnostic investigation of choice?

A	Blood cultures
B	CRP
C	Knee X-ray
D	Uric acid
E	Synovial fluid examination

## Explanation

The answer is Synovial fluid examination

In this situation the differential is between septic arthritis and gout. Whilst uric acid may be elevated it does not necessarily rule in gout or rule out septic arthritis. Knee X-ray in an obese man is likely to show osteoarthritic changes and little else, and even in septic arthritis, blood cultures are likely to have a low diagnostic yield. CRP may be elevated in both inflammatory and infective arthritis, so again is not useful as a differentiator. Acute management of gout includes use of NSAIDs, colchicine, or corticosteroids. The mainstay of chronic management is use of xanthine oxidase inhibitors, with or without uricosuric agents.



A 22-year-old man complains of an acute onset of pain in his right elbow and both Achilles tendons. He also gives history of dysuria, conjunctivitis and fever. He returned from holiday in the Far East 3 weeks ago, where he had unprotected sex. He has developed macules and pustules on his hands and feet.

What is the most likely diagnosis?

A	Gonococcal arthritis
B	HIV
C	Reactive arthritis
D	Psoriatic arthritis
E	Syphilitic arthritis

## Explanation

### Reactive arthritis (formerly known as Reiter syndrome)

Reactive arthritis comprises the triad of non-specific urethritis, conjunctivitis and arthritis. It may follow bacterial dysentery or exposure to sexually transmitted infection. In addition, patients may have Achilles tendinitis or plantar fasciitis. Other features are circinate balanitis and keratoderma blennorrhagica (macules, vesicles or pustules on the hands and feet). Patients may develop subungual hyperkeratosis and nail dystrophy.

A 44-year-old man with coeliac disease presents with pain in his hips and thighs. A hip X-ray shows linear areas of low density surrounded by sclerotic borders.

What is the most likely diagnosis?

- |   |                        |
|---|------------------------|
| A | Osteoporosis           |
| B | Osteomalacia           |
| C | Paget's disease        |
| D | Enteropathic arthritis |
| E | Reactive arthritis     |



# Explanation

## Osteomalacia

Osteomalacia occurs because of inadequate mineralisation of bone matrix. Malabsorption due to coeliac disease can lead to vitamin D deficiency. The X-ray picture is typical, showing the presence of Looser's zones (linear areas of low density surrounded by sclerotic borders).

### Differential diagnosis

- + In osteoporosis, the bone is normally mineralised, but deficient in quality, quantity and structural integrity.
- + Paget's disease is associated mainly with sclerosis, with bone expansion and loss of distinction between cortex and trabeculae (dedifferentiation).
- + Reactive arthritis is a sterile synovitis occurring following an infection such as bacillary dysentery due to *Shigella* or *Salmonella* spp., or diarrhoea due to *Yersinia enterocolitica*. X-rays are usually normal in this condition.
- + Enteropathic arthritis is usually associated with inflammatory bowel diseases such as ulcerative colitis or Crohn's disease.

A 70-year-old man attends the Rheumatology Clinic complaining of a stiff, painful right hand and pain and swelling in both knees. On examination, bony lumps are seen at the distal interphalangeal joints.

What is the most probable diagnosis?

A Rheumatoid arthritis

B Osteoarthritis

C Reiter syndrome

D Psoriatic arthritis

E Pseudogout

# Explanation

## Osteoarthritis

The bony lumps are Heberden's nodes and are seen in osteoarthritis. Osteoarthritis is the commonest form of arthritis. There is a strong association with age. Typically it affects the knee and hip joints. Hip, hand and generalised osteoarthritis are only prevalent in white people.

### Differential diagnosis

- + In rheumatoid arthritis there is a gradual onset of symmetrical arthralgia and synovitis of the small joints of the hands, feet and wrists. There is swelling of the metacarpophalangeal and proximal interphalangeal joints.
- + Reiter syndrome (now more commonly called reactive arthritis) manifests with the classic triad of non-specific urethritis, conjunctivitis and reactive arthritis. It is predominantly a disease of young men, with a ratio of men to women of 15:1.
- + Psoriatic arthropathy affects the distal interphalangeal joints and is almost invariably associated with nail dystrophy. Some 70% of patients will have a current or past history of previous skin lesions.
- + Pseudogout occurs due to the deposition of calcium pyrophosphate dihydrate crystals (chondrocalcinosis) in the large joints, particularly in the knees.



A 27-year-old man presents with upper-limb pain that is exacerbated by coughing or exercise. He has also noticed a weakness in his lower limbs and difficulty in walking. On examination, his fingernails are dystrophic and there is loss of upper limb reflexes.

What is the most likely diagnosis?

A	Thoracic disc prolapse
B	Psoriatic arthropathy
C	Syringomyelia
D	Ankylosing spondylitis
E	Adult polymyositis

A Thoracic disc prolapse

B Psoriatic arthropathy

C Syringomyelia

D Ankylosing spondylitis

E Adult polymyositis

# Explanation

## Differential diagnosis of upper-limb pain

- + The clinical features in this scenario are suggestive of syringomyelia, which is the development of a fluid-filled cavity or syrinx within the spinal cord. This produces a combination of long tract signs, notably lower limb spasticity and extensor plantar responses, in association with signs at the level of the syrinx, characteristically dissociated sensory loss and lower motor neurone signs such as clawing of the hand due to extension to anterior horn cells ('upper motor neurone signs in the lower limbs and lower motor neurone signs in the upper limbs').
- + Thoracic disc prolapse is uncommon in young adult males and would not cause weakness in the upper limbs.
- + Nail dystrophy may occur in psoriasis but this disease typically causes distal interphalangeal arthritis. Limb reflexes are not affected and weakness of limbs does not occur.
- + Ankylosing spondylitis classically affects young adult males. The features are low back pain and stiffness, worse in the morning and relieved by exercise. Uveitis and costochondritis may accompany this condition, but upper limb involvement with weakness and loss of reflexes is not seen.
- + Adult polymyositis is much more common in women (3:1) and usually presents with malaise, weight loss and fever. Proximal muscle weakness affecting shoulder and pelvic girdle muscles is progressive. Pain and tenderness are uncommon.



A 25-year-old woman complains of a loss of appetite, low-grade fever, pain in the shoulders and buttocks and severe cramping pain in her arms and hands while exercising. On examination the radial pulse is weak in both arms. The blood pressure is 85/60 mmHg in her right arm, 60/40 mmHg in her left arm and 130/80 mmHg in both legs.

What is the most likely diagnosis?

A	Takayasu's disease
B	Coarctation of the descending aorta
C	Cervical rib syndrome
D	Polyarteritis nodosa
E	Churg-Strauss syndrome

# Explanation

## Takayasu's disease

Takayasu's disease is an idiopathic arteritis that affects the first few centimetres of the innominate, carotid and subclavian arteries, together with the adjacent portion of the aorta. The typical patient is a woman aged 20-40 years. Blood pressure and pulse variations are common, as are systolic murmurs above and below the clavicle.

### Differential diagnosis

- + Coarctation of the descending aorta would cause reduced pulsation and blood pressure in the lower limbs.
- + Congenital development of the costal process of the C7 vertebra (cervical rib) can cause thoracic outlet compression. This involves the lowest trunk of the brachial plexus and the subclavian artery. Pain and numbness may be felt in the hand. The radial pulse may be weak and the forearm cyanosed. Other systemic symptoms would be absent in this condition.
- + Polyarteritis nodosa (PAN) is a necrotising vasculitis that causes aneurysms of medium-sized arteries. Abdominal pain due to infarction of a viscus, dyspnoea due to pulmonary infiltrates, arthralgia and purpuric spots can occur in this condition.
- + The Churg-Strauss syndrome is a variant of PAN, and characterised by lung involvement with pulmonary infiltrates.

A 61-year-old man with a history of ischaemic heart disease, including a recent inferior MI treated by stenting, comes to the Gastroenterology Clinic for review. He has been discharged a few weeks earlier following a haematemesis caused by a duodenal ulcer. He is H pylori negative although continues to complain of some indigestion. Other medical history of note includes rheumatoid arthritis, and his medication history includes Ramipril, Atorvastatin, Clopidogrel, Aspirin, Methotrexate and Folic acid. Clinical examination is unremarkable.

Which of the following is the most appropriate step to prevent further peptic ulcer disease?

A	Lansoprazole
B	Omeprazole
C	Ranitidine
D	Sodium alginate
E	Stop Aspirin



## Explanation

The answer is Lansoprazole -

It is clear that this patient still has symptoms of indigestion, is *H. pylori* negative and needs dual anti-platelet therapy because of the recent stenting. As such the only realistic option is to add a PPI. The potential for interaction reducing the effectiveness of Clopidogrel when it is co-prescribed with Omeprazole has now been recognised, leaving Lansoprazole as the only potential correct answer. Sodium alginate is most useful for the treatment of gastro-oesophageal reflux disease, and Ranitidine is inferior with respect to mucosal healing versus PPI.

A 42-year-old obese woman with a 10-year history of rheumatoid arthritis has been on prednisolone for a number of years. She presents with severe hip pain of relatively sudden onset and is now unable to walk. There is no history of even minor trauma.

What is the most probable diagnosis?

A	Flare-up of rheumatoid arthritis
B	Osteoarthritis
C	Pathological fracture of the femoral neck
D	Avascular necrosis of the femoral head
E	Meralgia paraesthetica

## Explanation

### Avascular necrosis of the femoral head

Long-term treatment with corticosteroids is a risk factor for avascular necrosis of the femoral head. A flare-up of rheumatoid arthritis is unlikely because her symptoms have been well controlled with prednisolone.

### Differential diagnosis

- + Osteoarthritis of the hip causes pain in the buttock and groin on standing and walking.
- + Pathological fracture of the femoral neck is usually due to osteoporosis, a condition that is usually postmenopausal.
- + Meralgia paraesthetica causes numbness and burning dysaesthesia over the anterolateral thigh. It may be precipitated by a sudden increase in weight. Inability to walk is not a feature of this condition, however.



A 60-year-old patient has been complaining of a 1-month history of generalised headache, malaise and fever. He has also noticed scalp sensitivity while brushing his hair.

Given the likely diagnosis, what would be the most appropriate treatment?

A	Aspirin
B	Oral corticosteroids
C	Topical corticosteroids
D	Clopidogrel
E	Dipyridamole

B	Oral corticosteroids
C	Topical corticosteroids
D	Clopidogrel
E	Dipyridamole

## Explanation

### Treatment of giant-cell arteritis

This patient presents with giant-cell arteritis, so corticosteroids are mandatory; immunosuppressive therapy has no direct effect and modest steroid-sparing rarely warrants the additional hazard.

While doses of prednisolone up to 100 mg per day are often advocated, careful sequential studies indicate that lower doses are quite satisfactory. Ophthalmologists, who are likely to see patients with established visual effects or threatening features in the second eye, might use higher doses or methylprednisolone infusions. Dosage reduction must be gradual and should be judged solely on clinical features as acute-phase responses are no guide. Most should have achieved a maintenance dose of 10 mg/day after 1 year.

The known persistence of disease in a significant proportion of patients for 4 years or more and the possible recurrence of symptoms, including blindness, even a year after corticosteroid withdrawal, argues for a very gradual reduction of dosage.

A 35-year-old woman presents with swollen and painful finger joints in both hands. You suspect rheumatoid arthritis and want to test for the presence of rheumatoid factor.

Which immunoglobulin is most commonly detected by routine testing?

A	IgG
B	IgA
C	IgM
D	IgE
E	IgD



A	IgG
B	IgA
C	IgM
D	IgE
E	IgD

## Explanation

### Rheumatoid factor

Rheumatoid factor is often present in patients with rheumatoid arthritis. This may be of any immunoglobulin class (IgM, IgG or IgA). The most common tests employed clinically detect IgM rheumatoid factor. Around 70% of patients with polyarticular rheumatoid arthritis have IgM rheumatoid factor in their serum. This is not diagnostic of rheumatoid arthritis, nor does its absence rule the disease out but it is a useful predictor of prognosis.

A 7-year-old boy presents with arthritis affecting his wrists, knees and ankles following an upper respiratory tract infection. He then develops scrotal swelling, melaena, renal impairment with haematuria and proteinuria and a rash affecting the lower limbs.

What is the most likely diagnosis?

A Henoch-Schönlein purpura (HSP)

B Polyarteritis nodosa

C Crohn's disease

D Reiter's syndrome

E Systemic lupus erythematosus

# Explanation

## Henoch-Schönlein purpura

The clinical scenario has enough information to diagnose Henoch-Schönlein purpura (HSP). Colicky abdominal pain is the classic symptom but melaena can occur. About 3% of patients develop significant renal disease. Approximately 50% of children have a history of preceding upper respiratory tract infection (URTI). The most common age at presentation for HSP is 4-15 years and there is a 2:1 male to female ratio.

Prednisolone treatment may be considered when there is significant renal disease; otherwise, only supportive care is often required. The prognosis is excellent in general, with most patients showing spontaneous recovery within 4 weeks.



A 65-year-old diabetic woman on indometacin and glibenclamide has had a blood test that shows evidence of renal failure, hyperkalaemia and hyperchloraemia.

What is the most likely underlying cause of her biochemical abnormalities?

- |   |                              |
|---|------------------------------|
| A | Acute interstitial nephritis |
| B | Renal artery stenosis        |
| C | Diabetic nephropathy         |
| D | Minimal-change nephropathy   |
| E | Renal tubular acidosis       |

# Explanation

## Renal tubular acidosis and NSAIDs

Hyperkalaemic, hyperchloraemic metabolic acidosis occurs in diabetic patients treated with indometacin. This is a form of distal renal tubular acidosis that is seen with non-steroidal anti-inflammatory drug (NSAID) administration.

## Differential diagnosis

- + Diabetic nephropathy characteristically presents with proteinuria. It is a gradually declining process that leads to renal failure after many years.
- + Acute interstitial nephritis is usually due to drug hypersensitivity and presents as acute renal failure, fever, arthralgia and eosinophilia. Hyperkalaemic, hyperchloraemic metabolic acidosis is not a feature of this condition.
- + Minimal-change nephropathy is typically seen in children and presents with nephrotic syndrome.
- + Renal artery stenosis is an important cause of hypertension that leads to renal failure. It can be caused by ACE inhibitors and angiotensin II receptor-blocking agents.

A 26-year-old woman complains that she has had a relapsing pain in her left ankle for the last 4–5 weeks. She also complains of a painful rash on the soles of her feet, and pain and swelling in her right toes. Over the last 2 weeks she has also developed low back pain. On further questioning she mentions that for the last few days she has noticed painless oral ulcers, which heal spontaneously. She also has a recent history of chlamydial urethritis in the last few months. Her full blood count and kidney and liver function tests are all normal. An autoimmune screen is negative.

What is the most likely diagnosis?

A	Reactive arthritis
B	Behcet's syndrome
C	Ankylosing spondylitis
D	Hypersensitivity vasculitis
E	Disseminated bacterial arthritis



# Explanation

## Presenting features of reactive arthritis

This woman has a recent history of chlamydial urethritis and now presents with arthritis. The painful sole is most likely due to plantar fasciitis, with the rash most likely to be keratoderma blenorrhagica, and fleeting and painless oral ulcers are well described in reactive arthritis. Conjunctivitis is part of the classic triad of reactive arthritis, and this can occur before or at the onset of arthritis. However other eye signs such as iritis can also occur. Asymmetric sacroiliitis presenting as backache occurs in about 20% of patients with reactive arthritis. The clinical spectrum of this condition is recognised to be wide and the term 'reactive arthritis' is now more frequently used (as opposed to its old nomenclature of Reiter syndrome); this encompasses the older concepts of complete and incomplete Reiter syndrome and a clinical syndrome of arthritis with or without extra-articular features following within 1 month of infectious diarrhoea or genitourinary infection.

A 35-year-old patient complains of feeling unwell for the last 6 months. He notices muscle weakness. On examination there is an erythematous scaly eruption confined to the skin overlying the knuckles. A random blood sample reveals a CK of 720.

What is the most likely diagnosis?

A Systemic lupus erythematosus

B Polymyositis

C Dermatomyositis

D Sjögren's syndrome

E Sarcoidosis

## Explanation

### Dermatomyositis

The unequivocal presence of Gottron's sign in association with proximal muscle weakness and elevation of muscle enzymes obviates the need for muscle biopsy because this picture is pathognomonic for dermatomyositis.



A 49-year-old woman presents to the Rheumatology Clinic for review. She has suffered from hypertension for some time, which has become less well controlled over the past year. Over the past 6 months she has also begun to suffer from Raynaud's phenomenon. On examination her BP is 152/85 mmHg; pulse is 75/min and regular. She has telangiectasia on her face, with evidence of skin thickening on her face and forearms, and calcinosis affecting her fingers. Respiratory examination is normal.

Investigations;

Hb	12.2 g/dl
WCC	$9.9 \times 10^9/l$
PLT	$201 \times 10^9/l$
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.5 mmol/l
Creatinine	95 micromol/l
Glucose	5.9 mmol/l
ESR	67 mm/1st hour
Urine	protein negative

Which of the following autoantibodies is most associated with this clinical presentation?

Which of the following autoantibodies is most associated with this clinical presentation?

A Scl-70

B Centromere

C RNA polymerase 3

D Anti-U1 RNP

E Anti-U3 RNP

## Explanation

The answer is Centromere -

Anti-centromere antibodies are seen in limited cutaneous systemic sclerosis. Limited systemic sclerosis is the most likely diagnosis here. Anti-Scl-70 antibodies are strongly associated with lung fibrosis, RNA polymerase 3 antibodies are found in diffuse cutaneous systemic sclerosis. U1-RNP is associated with joint disease, U3-RNP with cardiac involvement, pulmonary hypertension and myositis. Calcium channel antagonists are commonly used to manage Raynaud's syndrome, with proton pump inhibitors a consideration where there is underlying gastro-oesophageal reflux disease. Cyclophosphamide is the most commonly used non-selective immunosuppressive in the management of systemic sclerosis.



A 67-year-old woman presents with a 3-month history of persistent malaise, anorexia, shoulder and hip pain and a weight loss of 7 kg. On examination there is mild painful limitation of the hip and shoulder motion but no weakness and only minor muscle pain on palpation.

What is the most likely diagnosis?

- |   |                        |
|---|------------------------|
| A | Polymyositis           |
| B | Multiple sclerosis     |
| C | Polymyalgia rheumatica |
| D | Sarcoidosis            |
| E | Fibromyalgia           |

# Explanation

## Polymyalgia rheumatica

Polymyalgia rheumatica (PMR) occurs characteristically in elderly women and presents as aching and morning stiffness in the proximal muscles. Frank pain however is only seen in 1/3<sup>rd</sup> of patients. Minor tenderness is seen in the muscles rather than in the joints, but this is much less marked as compared to other conditions such as polymyositis. PMR is a form of giant-cell arteritis. The diagnosis is made on the basis of the history and symptoms. The erythrocyte sedimentation rate (ESR) is almost always remarkably high (> 40 mm in 1st hour).

### Differential diagnosis

- + Symmetrical proximal muscle weakness resulting from muscle inflammation is seen in polymyositis. Around 25% of patients have a purple (heliotrope) rash on the cheeks, eyelids and light-exposed areas (dermatomyositis). Dysphagia, dysphonia and respiratory weakness can develop
- + Sarcoidosis presents classically as bilateral hilar lymphadenopathy on chest X-ray. In a third of cases it presents with cough, fever, arthralgia, malaise or erythema nodosum. These are painful erythematous nodular lesions on the anterior aspect of the shins
- + Fibromyalgia classically presents with diffuse pain and multiple tender spots all over the body that may be unrelated to the affected muscles

A 24-year-old Nigerian complains of right hip pain. Blood tests show a haemoglobin level of 8.0 g/dl and the blood film shows target cells, sickle cells and reticulocytes. An X-ray shows loss of the right femoral head with periarticular sclerosis.

What is the most likely diagnosis?

A	Osteomyelitis
B	Perthe's disease
C	Osteoporosis
D	Septic arthritis
E	Avascular necrosis



# Explanation

## ✚ Avascular necrosis

Absence of the right femoral head on X-ray is consistent with avascular necrosis. This is a known complication of sickle cell disease. This condition results from a single glutamic acid to valine substitution at position 6 of the  $\beta$ -globin polypeptide chain. The greatest prevalence is in Africa, where the heterozygote frequency is over 20%. It may lead on to secondary osteoarthritis.

Perthes' disease is osteochondritis of the femoral head in children aged 3-11 years. It is bilateral in 10% of cases.

A 35-year-old man presents with abdominal pain, joint pains, fever and weight loss. He gives a history of passing bulky, malodorous stools over the past month that are difficult to flush away. A biopsy of the small bowel shows stunted villi with PAS- (Periodic acid-Schiff-) positive macrophages.

What is a characteristic finding in this condition?

A	Occult blood in stools
B	The presence of bacilli within macrophages on electron microscopy
C	Mesenteric thickening with lymph node enlargement on CT scan
D	Positive HLA-B27
E	Bony erosions and subluxation of joints on X-ray of affected joints

A	Occult blood in stools
B	The presence of bacilli within macrophages on electron microscopy
C	Mesenteric thickening with lymph node enlargement on CT scan
D	Positive HLA-B27
E	Bony erosions and subluxation of joints on X-ray of affected joints

## Explanation

### Whipple's disease

This patient has Whipple's disease. Peripheral arthritis occurs in 15% of patients. The disease is associated with steatorrhoea and abdominal pain. Occult blood is not seen in the stools. Transverse ulceration seen on a barium meal follow-through and mesenteric thickening with lymph node enlargement are characteristic of intestinal tuberculosis. Stunted villi with PAS- (Periodic acid-Schiff-) positive macrophages are seen in this condition. There is no particular association of Whipple's disease with HLA-B27.

Bony erosions and subluxations are a feature of rheumatoid arthritis.



A 45-year-old white woman complains of sudden back pain radiating down to her ankles. Her menstrual periods are regular. On examination, there is sensory loss over the soles of her feet and calves but the right side is much worse than the left. The straight leg-raising test is positive. Her body mass index (BMI) is 34 kg/m<sup>2</sup>. Routine blood tests are normal.

What is the most likely diagnosis?

- |   |                      |
|---|----------------------|
| A | Osteoarthritis       |
| B | Spinal stenosis      |
| C | Lumbar disc prolapse |
| D | Osteoporosis         |
| E | Osteomalacia         |

C	Lumbar disc prolapse
D	Osteoporosis
E	Osteomalacia

## Explanation

### Differential diagnosis of back pain

- + Lumbar disc prolapse is the correct diagnosis. This may have occurred as a result of her obesity (a body mass index of  $> 30 \text{ kg/m}^2$  indicates obesity).
- + Osteoarthritis may cause localised back pain but there would be no radiation down to the ankles and no sensory loss.
- + Osteomalacia is rare in developed countries but may be seen in high-risk groups such as female Muslim immigrants and elderly housebound people. In osteomalacia the alkaline phosphatase level is raised, along with raised parathyroid hormone levels and low levels of 25-hydroxycholecalciferol.
- + Osteoporosis is also unlikely in this patient, who has regular periods.
- + Spinal stenosis is a disease of the elderly where the classical presentation is pseudoclaudication, ie discomfort or pain in the legs on walking that is relieved by rest and by bending forwards. The straight leg-raising test is usually negative in those with spinal stenosis.

A 40-year-old woman presents with a 6-month history of pain and swelling of the proximal interphalangeal joints of both hands. A clinical diagnosis of rheumatoid arthritis is suspected. Which one of the following findings on blood testing is most likely to be seen in association with rheumatoid arthritis?

A Normochromic normocytic anaemia

B Neutropaenia

C Macrocytosis

D High antinuclear antibody levels

E HLA-B27



A	Normochromic normocytic anaemia
B	Neutropaenia
C	Macrocytosis
D	High antinuclear antibody levels
E	HLA-B27

## Explanation

### Blood test parameters in rheumatoid arthritis

The following features might be seen:

- + The full blood count may show anaemia of chronic disease or hypochromasia (due to gastrointestinal bleeding caused by drugs)
- + Neutropaenia occurs in Felty syndrome
- + A third of patients with rheumatoid arthritis have low titres of antinuclear antibody (ANA)
- + The erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) level are raised in proportion to the activity of the inflammatory process and are useful in monitoring treatment

HLA-B27 is not known to be associated with rheumatoid arthritis.

A 33-year-old woman is diagnosed with systemic lupus erythematosus (SLE) on the basis of polyarthralgia, mouth ulcers and antinuclear antibody (ANA) and anti-Ro antibody positivity. The urea and electrolytes are normal, the erythrocyte sedimentation rate (ESR) is 90 mm in 1st hour and urinalysis is normal.

How would you manage her?

- |   |  |
|---|--|
| A | Prednisolone 10 mg/day                           |
| B | Prednisolone 30 mg/day                           |
| C | Hydroxychloroquine 200 mg/day                    |
| D | Six monthly pulses of cyclophosphamide (2 mg/kg) |
| E | Nystatin drops                                   |

- |   |  |
|---|--|
| A | Prednisolone 10 mg/day                           |
| B | Prednisolone 30 mg/day                           |
| C | Hydroxychloroquine 200 mg/day                    |
| D | Six monthly pulses of cyclophosphamide (2 mg/kg) |
| E | Nystatin drops                                   |

## Explanation

### Treatment of systemic lupus erythematosus

In the absence of serious internal organ involvement (renal, neurological, eye or lung) there is no indication for cyclophosphamide or prednisolone. Simple arthralgia and fatigue appear to respond well to hydroxychloroquine.



A 4-year-old girl with a 1-day history of increasing hip pain is unable to stand. Her white cell count (WCC) is  $20 \times 10^9/l$ , erythrocyte sedimentation rate (ESR) 90 mm in 1st hour and C-reactive protein (CRP) 275 mg/l. A radiograph of the hip shows a widened joint space.

What is the most likely diagnosis?

A	Perthe's disease
B	Slipped upper femoral epiphysis
C	Septic arthritis
D	Congenital dislocation of hip
E	Osteomyelitis

B	Slipped upper femoral epiphysis
C	Septic arthritis
D	Congenital dislocation of hip
E	Osteomyelitis

## Explanation

### The painful hip in a child

- + The features are suggestive of septic arthritis. A painful, hot, swollen joint with increased synovial fluid, indicated by the widened joint space on X-ray, is characteristic of this condition.
- + Perthes' disease is osteochondritis of the femoral head and affects children aged between 3 and 11 years. It presents with pain in the hip or knee and causes a limp.
- + Slipped upper femoral epiphysis affects children aged 10–16 years and is bilateral in 20%. About half the patients are obese and hypogonadal.
- + Congenital dislocation of the hip is seen in neonates. Girls are more commonly affected than boys. If not detected in infancy, older children can present with delay in walking, an abnormal waddling gait and an inability to fully abduct the affected hip.
- + The distal femur and upper tibia are the common sites for osteomyelitis. Although X-ray changes are not apparent for a few days, they then show haziness and loss of density of the affected bone, followed by subperiosteal reaction and, later on, sequestrum and involucrum.

A 30-year-old woman with systemic lupus erythematosus (SLE) is eager to find out if she has any predisposing factors for the disease.

Which one of the following carries the highest risk?

- |   |   |
|---|---|
| A | Dizygotic twin of a patient with SLE        |
| B | First-degree relative of a patient with SLE |
| C | Monozygotic twin of a patient with SLE      |
| D | Positive HLA-B8                             |
| E | Positive HLA-DR2                            |



- |   |   |
|---|---|
| A | Dizygotic twin of a patient with SLE          |
| B | First-degree relative of a patient with SLE   |
| C | <b>Monozygotic twin of a patient with SLE</b> |
| D | Positive HLA-B8                               |
| E | Positive HLA-DR2                              |

## Explanation

### Genetic factors and SLE

There is a higher concordance rate in monozygotic twins (up to 25%) compared to dizygotic twins (up to 3%) in systemic lupus erythematosus (SLE). First-degree relatives have a 3% chance of developing the disease. There is an increased frequency of HLA B8 in white populations. There is a stronger association with HLA DR2 in Japanese people with lupus.

A 29-year-old woman presents to the Emergency Department with severe lethargy and joint pains. She has found it increasingly difficult to cope with her job over the past few weeks because of tiredness and her GP has arranged a number of blood tests. She has come to the department on this occasion because she has developed a rash affecting her buttocks and lower legs that she is finding it increasingly difficult to deal with. On examination she has a BP of 122/92 mmHg, pulse is 80/min and regular, her temperature is 37.9°C. There is an obvious small joint polyarthrititis, and a petechial rash affecting her buttocks, with a number of blisters over both lower limbs.

Investigations;

Hb	10.1 g/dl
WCC	11.3 x10 <sup>9</sup> /l
PLT	151 x10 <sup>9</sup> /l
ESR	87 mm/1 <sup>st</sup> hour
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	112 micromol/l (up from 90micromol/l at GP's some 2 weeks earlier)
Albumin	31 g/l
Urine	blood +, protein +
Anti-nuclear antibody	positive

Which of the following is the most appropriate intervention?

- A Admit for IV methylprednisolone
- B Ciclosporin
- C High dose oral Prednisolone
- D Low dose oral Prednisolone
- E No intervention but refer urgently to rheumatology



## Explanation

The answer is High dose oral Prednisolone -

This patient has SLE with renal involvement. In this situation with relatively normal renal function, the patient can be managed as an outpatient. She does however require treatment with high dose oral Prednisolone. Hydroxychloroquine is useful in addition to Prednisolone, particularly where there is significant joint disease, and Cyclophosphamide is considered for patients with life threatening lupus nephritis. Cyclosporin and Azathioprine are potential alternatives to Hydroxychloroquine as a steroid-sparing agent.

A 30-year-old woman visits your clinic with a 2-month history of pain in both her hands. Which symptom in her history is most characteristic of active rheumatoid arthritis?

- A Inability to knit because of pain in her fingers
- B Feels tired and unwell
- C Swelling of the finger joints
- D Marked stiffness for more than an hour in the mornings
- E Presence of firm non-tender nodules in the fingers and on the elbows

- |   |  |
|---|--|
| A | Inability to knit because of pain in her fingers                     |
| B | Feels tired and unwell   |
| C | Swelling of the finger joints  |
| D | Marked stiffness for more than an hour in the mornings               |
| E | Presence of firm non-tender nodules in the fingers and on the elbows |

## Explanation

Early symptoms of rheumatoid arthritis

Morning stiffness is a classic feature of rheumatoid arthritis, which may be prolonged for up to an hour or more. Subcutaneous nodules occur in 25% of cases.

Loss of joint mobility, pain and malaise and swelling of the finger joints are common to all arthritides.



A 52-year-old woman comes for review. She has a symmetrical small-joint polyarthritis affecting predominantly the proximal interphalangeal joints, both knees and ankles. Her pain is predominantly worst in the morning, when she also has significant stiffness. Investigations show: haemoglobin 12.1 g/dl, white cell count  $5.2 \times 10^9/l$ , platelets  $190 \times 10^9/l$ , sodium 139 mmol/l, potassium 5.0 mmol/l, creatinine 105  $\mu\text{mol/l}$ , rheumatoid factor +++.

What X-ray changes would you expect to see in the hands?

- |   |   |
|---|---|
| A | Osteophyte formation                                  |
| B | Periarticular osteopaenia around the PIP joints       |
| C | Periarticular sclerosis around the DIP joints         |
| D | Cyst formation in the distal portion of the phalanges |
| E | Carpal bone micro fractures                           |

- |   |   |
|---|---|
| A | Osteophyte formation                                  |
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| C | Periarticular sclerosis around the DIP joints         |
| D | Cyst formation in the distal portion of the phalanges |
| E | Carpal bone micro fractures                           |

## Explanation

### Diagnostic imaging of the hand

The proximal interphalangeal joints are more commonly affected in rheumatoid arthritis, and periarticular osteopenia is a feature seen in association with rheumatoid arthritis. Other features seen include bony erosions, cyst formation, and joint-space narrowing/swelling. Where the diagnosis is in doubt, joint-space aspiration of large joints can be considered to determine whether an inflammatory arthritis is present. Initial therapy is based on use of non-steroidal anti-inflammatory drugs, with or without the addition of disease-modifying anti-rheumatoid drugs (DMARDs), according to therapeutic response.

A 26-year-old woman presents with a malar rash, photosensitivity and arthralgia. On examination she has oral ulcers and her urine dipstick shows haematuria and proteinuria.

What is the most likely diagnosis?

- |   |                              |
|---|------------------------------|
| A | Rheumatoid arthritis         |
| B | Systemic lupus erythematosus |
| C | Behçet's disease             |
| D | Polymyalgia rheumatica       |
| E | Systemic sclerosis           |



# Explanation

## Systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a chronic condition in which a low level of baseline activity is punctuated by flares of higher activity. The overall severity of the disease in a particular patient depends on the nature and frequency of these flares.

## Clinical features

The diverse clinical features of SLE mean that the disease may present to any of a number of different specialists, including rheumatologists, dermatologists, nephrologists and general physicians. SLE may be diagnosed if a patient meets at least four of the following 11 criteria:

- + Malar rash
- + Discoid rash
- + Photosensitivity
- + Oral ulcers
- + Arthritis
- + Serositis (pleuritis or pericarditis)
- + Renal disorder (proteinuria  $> 0.5$  g/24 hours, or +++ persistently or cellular casts)
- + Neurological disorder (seizures or psychosis)
- + Haematological disorder (haemolytic anaemia or leukopenia of  $4.0 \times 10^9/l$  on two or more occasions, or lymphopenia of  $1.5 \times 10^9/l$  on two or more occasions, or thrombocytopenia of  $100 \times 10^9/l$ )
- + Immunological disorders (raised anti-native DNA antibody-binding or anti-Sm antibody or positive finding of antiphospholipid antibodies)
- + Antinuclear antibody in raised titre (in the absence of drugs known to be associated with drug-induced lupus)



You review a 59-year-old woman with a history of deteriorating vision. You diagnose the patient to have ischaemic optic atrophy.

Ischaemic optic atrophy is most likely to be associated with which one of the following diseases?

A	Rheumatoid arthritis
B	Wegener's granulomatosis
C	Systemic lupus erythematosus
D	Seronegative arthritis
E	Still's disease

A	Rheumatoid arthritis
B	Wegener's granulomatosis
C	Systemic lupus erythematosus
D	Seronegative arthritis
E	Still's disease

## Explanation

### Ischaemic optic atrophy in rheumatic diseases

Ischaemic optic atrophy is not routinely seen in patients with rheumatoid arthritis but may be a major ophthalmic manifestation of giant-cell arteritis, Wegener's granulomatosis and, less commonly, systemic lupus erythematosus (SLE). Optic atrophy is not usually seen in association with Still's disease.

Other causes of optic atrophy include secondary optic atrophy after papilloedema, demyelinating optic neuritis as seen in multiple sclerosis, vitamin B<sub>12</sub> deficiency, quinine and methyl alcohol ingestion. The degree of visual loss depends on the underlying cause. Hereditary causes of optic atrophy include Leber's hereditary optic neuropathy (a mitochondrial disorder).

A 35-year-old patient complains of feeling unwell for the last 6 months. He has noticed a malar rash and weakness of his proximal muscles. On examination there is an erythematous scaly eruption over the extensor surfaces of his arms. His creatine kinase is elevated.

What is the next step in obtaining the diagnosis?

- |   |                       |
|---|-----------------------|
| A | Hand X-ray            |
| B | Muscle biopsy         |
| C | Nerve conduction test |
| D | Abdominal ultrasound  |
| E | Rheumatoid factor     |



A	Hand X-ray
B	Muscle biopsy
C	Nerve conduction test
D	Abdominal ultrasound
E	Rheumatoid factor

## Explanation

### Diagnosis of dermatomyositis

In cases of possible polymyositis or dermatomyositis confirmation of the diagnosis by muscle biopsy is essential. Other studies, such as electromyography, nerve conduction studies and magnetic resonance imaging are adjuncts to diagnosis but do not supplant tissue biopsy.

The unequivocal presence of Gottron's sign (an erythematous, scaly eruption confined to skin overlying the knuckles) in association with proximal muscle weakness and elevation of muscle enzymes obviates the need for muscle biopsy because it is pathognomonic. Identical lesions known as 'Gottron's papules' also occur over the extensor surfaces of many other joints, particularly the elbows and knees.

A 25-year-old man presents in the Emergency Department with a 2-day history of a painful and swollen left knee. He is pyrexial, with a temperature of 38.5 °C. Examination of his cardiovascular and respiratory system is normal. An abdominal examination is normal. He also mentions that he developed a painful right ear and saw his doctor 5 days ago, who told him he had an infected ear and prescribed antibiotics. His left knee is swollen, red, tender and slightly flexed. A diagnosis of septic arthritis is made.

What is the most likely causative organism?

- |   |                                   |
|---|-----------------------------------|
| A | <i>Streptococcus viridans</i>     |
| B | <i>Staphylococcus epidermidis</i> |
| C | <i>Staphylococcus aureus</i>      |
| D | <i>Escherichia coli</i>           |
| E | <i>Neisseria meningitides</i>     |

- |   |                                   |
|---|-----------------------------------|
| A | <i>Streptococcus viridans</i>     |
| B | <i>Staphylococcus epidermidis</i> |
| C | <i>Staphylococcus aureus</i>      |
| D | <i>Escherichia coli</i>           |
| E | <i>Neisseria meningitides</i>     |

## Explanation

### Septic arthritis

#### Pathophysiology

Septic arthritis results from infection of the joints with pyogenic organisms, of which *Staphylococcus aureus* is the commonest. Other organisms responsible are streptococci, *Neisseria* spp. and Gram-negative bacilli. The organisms reach the joint via the bloodstream, sometimes from known sites of infection such as boils or otitis media. Less commonly, it may spread from osteomyelitis adjacent to the joint or it may be introduced into the joint as a result of trauma.



## Clinical features

The patient complains of a single painful joint, which appears red, warm and swollen.

Diagnosis: Aspirating the joint and examining and culturing the fluid should establish diagnosis.

Treatment should be started immediately with appropriate antibiotics as delays can result in destruction of the cartilage. The joint should be immobilised. The joint should be drained by needle aspiration. Inaccessible joints such as the hip may require surgical drainage.



A 47-year-old woman with a 15-year history of rheumatoid arthritis presents with a red, swollen and hot knee joint. A provisional diagnosis of septic arthritis is made.

Which organism is most commonly responsible for this condition?

A *Streptococcus pyogenes*

B *Haemophilus influenzae*

C *Staphylococcus aureus*

D *Neisseria gonorrhoeae*

E *Escherichia coli*

A *Streptococcus pyogenes*

B *Haemophilus influenzae*

C *Staphylococcus aureus*

D *Neisseria gonorrhoeae*

E *Escherichia coli*

## Explanation

### Septic arthritis

The organism that most commonly causes septic arthritis is *Staphylococcus aureus*. Gram-negative organisms are more commonly seen in the elderly or complicating rheumatoid arthritis and *Haemophilus influenzae* infection is seen more often in children.

A 44-year-old, diabetic, obese man presents with a painful swollen ankle that has become worse over the past 2 weeks. He gives a history of recent alcohol consumption. Small rhomboid-shaped crystals are seen in the joint aspirate, along with numerous neutrophils. An X-ray shows evidence of chondrocalcinosis.

What is the most likely diagnosis?

A	Gouty arthritis
B	Osteoarthritis
C	Septic arthritis
D	Charcot's joint
E	Pseudogout

# Explanation

## Pseudogout

Small, rhomboid-shaped, weakly positive birefringent crystals are seen in calcium pyrophosphate arthropathy (pseudogout). Calcification of joint cartilages (chondrocalcinosis) is a feature of this disease. The joint aspirate may show numerous neutrophils.

Charcot's deformity arises in weight-bearing joints (mainly the ankles) and may be due to neurovascular changes rather than simple neurotrauma. It is most commonly associated with chronic sensory neuropathies, such as occur in diabetes mellitus, tertiary syphilis and syringomyelia.



A 40-year-old man presents with haematuria and recurrent haemoptysis. Blood tests are positive for ANCA-PR3 and ANCA-MPO. The eosinophil count is  $0.3 \times 10^9/l$  (normal range  $0.04\text{--}0.4 \times 10^9/l$ ).

What is the most probable diagnosis?

- |   |                              |
|---|------------------------------|
| A | Wegener's granulomatosis     |
| B | Churg-Strauss syndrome       |
| C | Goodpasture's syndrome       |
| D | Microscopic polyangiitis     |
| E | Cryoglobulinaemic vasculitis |

- |   |                              |
|---|------------------------------|
| C | Goodpasture's syndrome       |
| D | Microscopic polyangiitis     |
| E | Cryoglobulinaemic vasculitis |

## Explanation

### ANCA antibodies

- + The presence of ANCA-PR3 and ANCA-MPO is characteristic of microscopic polyangiitis (where ANCA-PR3 = antineutrophil cytoplasmic antibody proteinase 3 and ANCA-MPO = antineutrophil cytoplasmic antibody myeloperoxidase).
- + ANCA-MPO is seen more rarely in Wegener's granulomatosis, but may be found in up to 20% of patients. Both antibodies are also present in Churg-Strauss syndrome. However, eosinophilia is a characteristic feature of Churg-Strauss syndrome while the eosinophil count in this patient is normal.
- + ANCA antibodies are not present in cryoglobulinaemic vasculitis.
- + Goodpasture syndrome is mediated by anti-glomerular basement membrane antibody. These are of IgG type.

A 30-year-old woman undergoes arthroscopy and joint fluid aspiration for suspected rheumatoid arthritis.

Which one of the following findings would best confirm the diagnosis?

A	Normal-looking synovial membrane
B	Increased viscosity of synovial fluid
C	Clear synovial fluid
D	Neutrophils in the aspirate on microscopy
E	Marked vascular proliferation on the synovial membrane

- |   |   |
|---|---|
| A | Normal-looking synovial membrane                              |
| B | Increased viscosity of synovial fluid                         |
| C | Clear synovial fluid  |
| D | Neutrophils in the aspirate on microscopy                     |
| E | <b>Marked vascular proliferation on the synovial membrane</b> |

## Explanation

### The synovial membrane in rheumatoid arthritis

Synovial membrane is almost always involved in rheumatoid arthritis. There is marked vascular proliferation with increased permeability of blood vessels on the synovial membrane that is typical of rheumatoid arthritis. Thickening of the synovial membrane and proliferation into folds and fronds may also be seen. The viscosity of synovial fluid is decreased. The fluid is turbid (with neutrophils) in earlier phases of the disease, but this is not a diagnostic feature.



A 47-year-old woman with a 15-year history of rheumatoid arthritis presents with fever, weight loss and leg ulcers. On examination she is found to have splenomegaly.

Which human leucocyte antigen (HLA) type is most common in patients with Felty syndrome versus patients without this condition?

A	HLA-B27
B	HLA-B8DR3
C	HLA-B51
D	HLA-DRW4
E	HLA-DR4

B	HLA-B8DR3
C	HLA-B51
D	HLA-DRW4
E	HLA-DR4

## Explanation

### HLA associations in rheumatology

- + This patient has Felty syndrome and this human leucocyte antigen (HLA) subtype (HLA DRW4) is found in 95% of patients with Felty syndrome compared with 70% of people with rheumatoid arthritis alone.
- + HLA-B8DR3 is associated with Sjögren syndrome.
- + HLA-B51 is more common in Behçet's disease.
- + Some HLA-B27 subtypes are associated with ankylosing spondylitis.
- + HLA-DR4 occurs in 50-75% of patients with rheumatoid arthritis and correlates with a poor prognosis; it is more likely to be found in patients with Felty syndrome, but is not as specific as DRW4.

A 50-year-old man who works as a carpet fitter comes to the clinic with a swollen, painful left knee. He has difficulty kneeling and walking and has been unable to work. This is the 4th attack he has had in the past 2 years and he is unable to modify his work. On examination he has tenderness, erythema and swelling over the patella, with severely reduced knee flexion.

Investigations;

Hb	13.1 g/dl
WCC	$7.8 \times 10^9/l$
PLT	$192 \times 10^9/l$
Na <sup>+</sup>	138 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	100 micromol/l
Pre-patellar bursa aspiration	>5000 white cells / microlitre (no growth)

Which of the following is likely to be the most effective treatment?

A	Arthroscopic bursectomy
B	Intra-articular corticosteroids
C	NSAIDs
D	Oral corticosteroids
E	Rest



## Explanation

The answer is Arthroscopic bursectomy

The position of the pain and swelling, (over the pre-patellar bursa), and results on aspiration confirm a diagnosis of "housemaid's knee". Diagnosis is based upon the results of fluid white count, lactate, glucose and examination for crystals. Mild elevation in bursa fluid white count may be seen in inflammatory bursitis, much greater rises can be seen in infective pre-patellar bursitis.

Realistically this man is not going to change his job, and recurrent attacks of pre-patellar bursitis are significantly impacting on his quality of life and his ability to continue to work. Intra-articular corticosteroids, NSAIDS and rest are all possible treatment options, but none are likely to provide him with a permanent solution. As such arthroscopic bursectomy is the logical next step.

A middle-aged man with long-standing rheumatoid arthritis presents with a red, swollen and hot right knee. His temperature is 39.2 °C.

What would be the best immediate management of this man?

- |   |  |
|---|--|
| A | Flucloxacillin and benzylpenicillin      |
| B | Blood culture                            |
| C | Joint aspiration, microscopy and culture |
| D | Oral prednisolone and physiotherapy      |
| E | Commence sulfasalazine                   |

- |   |  |
|---|--|
| A | Flucloxacillin and benzylpenicillin      |
| B | Blood culture                            |
| C | Joint aspiration, microscopy and culture |
| D | Oral prednisolone and physiotherapy      |
| E | Commence sulfasalazine                   |

## Explanation

### Septic arthritis

This patient has septic arthritis. The most likely organism is *Staphylococcus aureus*, particularly in patients with rheumatoid arthritis and diabetes mellitus. Joint aspiration is essential whenever septic arthritis is suspected. Synovial fluid culture is positive in 90% of cases. Empirical antibiotic therapy with flucloxacillin is commenced until culture sensitivity results are available.

A 52-year-old man comes to the Emergency Department with a sore throat and fever. He is currently treated with a disease-modifying agent for rheumatoid arthritis but he cannot remember the name of it, and has recently been prescribed Allopurinol for gout. On examination he is pyrexial 38.2°C, and has obvious pharyngitis. He is neutropenic with a neutrophil count of  $0.4 \times 10^9/\text{l}$ .

Which of the following agents is he most likely to have been treated with for his arthritis?

A	Azathioprine
B	Ciclosporin
C	Hydroxychloroquine
D	Infliximab
E	Methotrexate



## Explanation

The answer is Azathioprine -

Allopurinol interferes with the metabolism of 6-mercaptopurine, the active metabolite of Azathioprine. This leads to a build up of 6-mercaptopurine, resulting in neutropenia. Patients who suffer gout whilst taking Azathioprine or 6-mercaptopurine should therefore not be prescribed Allopurinol or should have their dose of disease modifying agent significantly reduced. Infliximab is recognised to increase the risk of TB, and Methotrexate leads to hepatic and pulmonary fibrosis.

A 72-year-old woman comes to the peripheral hospital clinic complaining of severe temporal headaches, jaw claudication on eating and an episode of visual blurring affecting her right eye. On further questioning she says that has had shoulder and pelvic girdle pain going back for a period of 6 months or so. She has a history of hypertension and osteoarthritis, and takes ramipril and regular paracetamol.

On examination she has a blood pressure of 160/95 mmHg and a pulse of 78 bpm. There is temporal artery tenderness to palpation. You have some basic bloods available which were sent in by her GP. Investigations show: haemoglobin 12.3 g/dl, white cell count  $7.2 \times 10^9/\text{l}$ , platelets  $199 \times 10^9/\text{l}$ , sodium 140 mmol/l, potassium 4.8 mmol/l, creatinine 132  $\mu\text{mol/l}$ . She is not able to come in for admission immediately because she needs to go home and sort out some household arrangements.

Which one of the following is the next most important step in her management?

A	Arrange CT head
B	Give her 60mg of oral prednisolone
C	Arrange to check her ESR when she returns
D	Book a temporal artery biopsy
E	Start her on diclofenac

- |   |   |
|---|---|
| A | Arrange CT head                           |
| B | Give her 60mg of oral prednisolone        |
| C | Arrange to check her ESR when she returns |
| D | Book a temporal artery biopsy             |
| E | Start her on diclofenac                   |

## Explanation

### First-line management of temporal arteritis

This woman is at risk of sight loss, her symptoms being entirely consistent with a diagnosis of temporal arteritis. Given that there may be an interval before she attends the hospital, where the erythrocyte sedimentation rate (ESR) can be checked and she can be referred for temporal artery biopsy, advice is not to delay treatment with corticosteroids. Visual damage is usually irreversible, with partial or complete sight loss occurring in 15% to 20% of patients with temporal arteritis. Chronic steroid treatment is the norm, with most patients treated for a period of longer than 6 months.



A 75-year-old woman with rheumatoid arthritis is being treated with methotrexate. She presents with malaise, fever and swelling and pain of her right wrist.

What is the most likely diagnosis?

A	Osteoarthritis
B	Joint sepsis
C	Pseudogout
D	Carpal tunnel syndrome
E	Gout



## Explanation

### Joint sepsis

This patient probably has joint sepsis. Methotrexate is usually given in cases of rheumatoid arthritis that do not respond satisfactorily to disease-modifying antirheumatic drugs (DMARDs). Marrow suppression is a feature of this therapy and this may result in infections.

Pseudogout or calcium pyrophosphate arthropathy is non-inflammatory and would not be associated with fever. Acute gouty arthritis is common in the metatarsophalangeal joint. It is not related to rheumatoid arthritis or to methotrexate treatment. Osteoarthritis would usually present in a weight-bearing joint and is not associated with malaise and fever. Carpal tunnel syndrome would present with pain and tingling, usually in the radial half of the hand. Fever does not occur in this condition.

A 29-year-old woman with a history of systemic lupus erythematosus (SLE) gives birth to her first child. The nurses are concerned because the newborn infant looks as if she has an SLE-like skin rash.

Which maternal autoantibody is most associated with the development of neonatal lupus?

- A Anti-Ro antibodies
- B Anti-cardiolipin antibodies
- C Anti-ds DNA antibodies
- D Anti-smooth muscle antibodies
- E Anti-La antibodies

A	Anti-Ro antibodies
B	Anti-cardiolipin antibodies
C	Anti-ds DNA antibodies
D	Anti-smooth muscle antibodies
E	Anti-La antibodies

## Explanation

### Fetal lupus

Fetal lupus is highly associated with anti-Ro antibodies, although there can also be an association with anti-La antibodies. Not all cases of fetal lupus are always seen in association with heart block; if this is suspected by measuring the pulse on an 18-week scan, then prophylactic dexamethasone may be an option. Rates of fetal loss are substantially higher in women suffering from lupus, and are associated with particularly high titres of anti-double-stranded DNA (anti-dsDNA).

A 19-year-old student presents with swelling of the face, hands and feet, together with diffuse abdominal pain. He gives a history of recurrent episodes since he was 10 years old, at a rate of three or four attacks per year. Each episode lasts 2-3 days. On examination swelling is observed at the above-mentioned sites but there is no evidence of urticaria. The family history reveals a history of similar episodes in the mother since childhood and in the older brother, who died of respiratory distress at the age of 8 years during a similar attack.

Which one of the following tests would be considered most helpful in establishing the diagnosis?

A	Eosinophil count in the blood
B	Prick (puncture) skin test
C	Radioallergosorbent test (RAST)
D	C1 esterase inhibitor (C1INH)
E	IgE levels



D

C1 esterase inhibitor (C1INH)

E

IgE levels

## Explanation

### Hereditary angioedema

Angioedema, characterised by non-pitting, erythematous swelling of soft tissues, can be hereditary or acquired. Hereditary angioedema (HAE) is an autosomal dominant disease due to mutations at C1 inhibitor gene. The defective gene does not produce sufficient levels of C1 inhibitor in plasma, which leads to auto-activation of C1 and consumption of C2 and C4. It is further classified into type I (lower production of C1 inhibitor proteins) and type II (functional defect of C1 inhibitor with normal plasma levels).

**Clinical presentation:** Hereditary angioedema is characterised by recurrent self-limited attacks involving the skin, subcutaneous tissue, upper respiratory tract or gastrointestinal tract. Attacks may last from several hours to 2-3 days. Gastrointestinal or upper respiratory tract attacks may be precipitated by local trauma (eg dental procedures, tonsillectomy).

**Investigation:** Hereditary angioedema is characterised by low levels of C1 esterase inhibitor (C1INH) or elevated levels of dysfunctional C1 esterase inhibitor, as detected by an immune assay. Low levels of C4 are seen between attacks.

Acquired angioedema maybe a manifestation of urticaria and has recently been described as a side-effect of drugs such as angiotensin-converting enzyme (ACE) inhibitors.

A 34-year-old woman with a history of arthritis of many years' duration that has deformed her hands presents with pain and colour changes in the fingers of both hands on exposure to cold, dryness in her mouth and a gritty sensation in her eyes.

From what complication affecting her mucous membranes/eyes is she suffering?

- |   |                                      |
|---|--------------------------------------|
| A | Arthritis mutilans                   |
| B | Reiter's syndrome                    |
| C | Systemic lupus erythematosus         |
| D | Diffuse cutaneous systemic sclerosis |
| E | Sjögren's syndrome                   |

# Explanation

## Sjögren syndrome

Sjögren syndrome is an autoimmune disorder of unknown aetiology characterised by lymphocytic infiltration of the salivary and lacrimal glands, leading to glandular fibrosis and exocrine failure. The age of onset is usually in the fourth and fifth decades, with a female to male ratio of 9:1. The disease may be primary or secondary in association with other autoimmune diseases (such as rheumatoid arthritis, systemic lupus erythematosus, thyroiditis or primary biliary cirrhosis). Dryness of the eye (keratoconjunctivitis sicca) may be demonstrated by Schirmer's test. Antinuclear antibody and rheumatoid factor are present in most cases.



A 45-year-old woman complains of feeling tired. She also notices she has dysphagia, a dry mouth, a gritty sensation in her eyes and increased photosensitivity.

What is the most likely diagnosis?

- |   |                             |
|---|-----------------------------|
| A | Sjögren syndrome            |
| B | Polymyositis                |
| C | Oesophageal carcinoma       |
| D | Haemochromatosis            |
| E | Hepatitis C virus infection |



# Explanation

## Sjögren syndrome

Sjögren syndrome is characterised by inflammation and the destruction of exocrine glands. The salivary and lacrimal glands are principally involved, giving rise to dry eyes and mouth. The aetiology of Sjögren syndrome is unknown but it is often considered to be an interaction between constitutional and environmental factors, leading to autoimmunity. Primary Sjögren syndrome is strongly associated with HLA DR3. Sjögren syndrome is nine times more common in women than men and can develop at any age from 15 to 65.

### Clinical features

Patients rarely complain of dry eyes, but rather of a gritty sensation, soreness, photosensitivity or intolerance to contact lenses. In early disease excessive watering or deposits of dried mucus in the corner of the eye and recurrent attacks of conjunctivitis can occur. The dry mouth is often manifest as the 'cream cracker' sign, an inability to swallow dry food without fluid or waking up in the night to take sips of water. About half of patients complain of intermittent parotid swelling, sometimes misdiagnosed as recurrent mumps. When the swelling is excessively painful it is often due to a secondary bacterial infection.

On examination, xerostomia can be detected as a diminished salivary pool, a dried fissured tongue, often complicated by angular stomatitis, and chronic oral candidiasis. The eyes might be reddened and roughened due to shallow erosions in the conjunctiva.

True Sjögren syndrome is a systemic disease. Some two-thirds of patients complain of fatigue, which, according to a recent epidemiological study, is the single most important cause of disability.

A 75-year-old woman, who is a chronic alcoholic, presents with recurrent episodes of a swollen, red-hot right ankle. Aspiration of the joint reveals negatively birefringent crystals.

What is the probable diagnosis?

- |   |  |
|---|--|
| A | Calcium pyrophosphate arthropathy        |
| B | Monosodium urate monohydrate arthropathy |
| C | Basic calcium phosphate deposition       |
| D | Osteoarthritis                           |
| E | Osteoporosis                             |

- |   |  |
|---|--|
| A | Calcium pyrophosphate arthropathy        |
| B | Monosodium urate monohydrate arthropathy |
| C | Basic calcium phosphate deposition       |
| D | Osteoarthritis                           |
| E | Osteoporosis                             |

## Explanation

### Gouty arthritis

This patient has acute attacks of gouty arthritis affecting her ankle. Secondary gout due to alcohol or drug intake mainly affects people over the age of 65 and is the form most commonly seen in women. Monosodium urate monohydrate (MSUM) crystals appear negatively birefringent under polarised light. The clinical presentation described is not seen in osteoarthritis or osteoporosis.



A 29-year-old professional dancer is referred to the clinic with a small joint polyarthrititis, which has continued to worsen over the past 8 weeks despite treatment with Ibuprofen and rest from work. The small joints of her hands and feet, wrists, ankles, knees and elbows are particularly affected. She takes no regular medication and has no significant past medical history. On examination her BP is 105/70 mmHg, pulse is 80/min and regular. Her BMI is 20.5. You confirm a small joint polyarthrititis in the pattern typical for rheumatoid arthritis.

Which of the following is the most important criterion to confirm the diagnosis?

A	Erosive changes on X-ray
B	Failure to respond to NSAID therapy
C	Joint symptoms for longer than 6 weeks
D	Positive rheumatoid factor
E	Presence of rheumatoid nodules



# Explanation

The answer is Joint symptoms for longer than 6 weeks -

The diagnosis of rheumatoid arthritis should be made as early as possible to allow patients to benefit from disease modifying therapies. As such once patients have symptoms for longer than a 6 week period, the diagnosis can usually be considered. Positive rheumatoid factor is not a definitive requirement, indeed anti-CCP antibodies may be more likely to be positive in the early stages of the disease.

Typical criteria for considering a diagnosis of rheumatoid are listed below; however it is important to note that not all are required.

- + Morning stiffness that lasts at least one hour and that has been present for at least six weeks
- + Swelling of three or more joints for at least six weeks
- + Swelling of the wrist, hand, or finger joints for at least six weeks
- + Swelling of the same joints on both sides of the body
- + Changes in hand x-rays that are characteristic of rheumatoid arthritis
- + Rheumatoid nodules of the skin
- + Blood test positive for rheumatoid factor and/or anti-citrullinated peptide/protein antibodies

A 15-year-old girl presents with pain and swelling over her right knee that has progressively worsened over the last 10 days. She is actively involved in sports and has recently been selected for national championships. Clinical examination reveals pain over the tibial tubercle, and an X-ray of the knee reveals fragmentation of the tibial tubercle.

What is the most likely cause of her condition?

A	Osteochondritis dissecans
B	Osgood-Schlatter's disease
C	Infrapatellar bursitis
D	Torn meniscus
E	Torn anterior cruciate ligament

- |   |                                 |
|---|---------------------------------|
| A | Osteochondritis dissecans       |
| B | Osgood-Schlatter's disease      |
| C | Infrapatellar bursitis          |
| D | Torn meniscus                   |
| E | Torn anterior cruciate ligament |

## Explanation

### Pain and swelling in a teenager's knee

- + Osgood-Schlatter disease causes pain and swelling over the tibial tubercle. A traction apophysitis of the patellar tendon, it is seen in sports players undergoing rigorous training
- + Osteochondritis dissecans is more common in adolescent and young adult males. Locking or giving way of the joint is seen in this condition
- + A twisting injury is a common history in meniscal tears. There is immediate medial or lateral knee pain and dramatic swelling develops within a few hours
- + A torn anterior cruciate ligament allows the tibia to be pulled forwards on the femur when the knee is flexed to 90°
- + Infrapatellar bursitis is caused by kneeling (housemaids' knee). There is local pain, tenderness and a fluctuant swelling



You are asked to see a 65-year-old Asian woman who is complaining of generalised body aches. Her daughter also mentions that for the last few months her mother has found it difficult to get up from a chair. She suffers from diet-controlled diabetes mellitus and her blood glucose level is well controlled. Her full blood count is normal. She has low serum phosphate, plasma calcium at the lower end of the normal range and raised alkaline phosphatase levels.

Which one of the following would you expect her X-rays to show?

A	Linear areas of low density
B	Increased bone density
C	Osteolytic areas with bone destruction
D	Brodie's abscess
E	Areas of sclerosis



A	Linear areas of low density
B	Increased bone density
C	Osteolytic areas with bone destruction
D	Brodie's abscess
E	Areas of sclerosis

## Explanation

### Osteomalacia

This woman has generalised body aches and also has features suggestive of proximal myopathy. The bone biochemistry is in keeping with a diagnosis of osteomalacia. X-rays will typically show defective mineralisation, especially in the pelvis, long bones and ribs. Areas of low density – Looser's zones – are characteristic of the condition.

A 38-year-old woman complains of generalised body pain. She sleeps well but does not feel refreshed in the morning. She is unable to exercise and feels tired all the time, cannot work and takes to her bed for much of the day.

What is the most likely diagnosis?

- |   |                          |
|---|--------------------------|
| A | Polymyositis             |
| B | Polymyalgia rheumatica   |
| C | Chronic fatigue syndrome |
| D | Multiple sclerosis       |
| E | Hypochondriasis          |

# Explanation

## Chronic fatigue syndrome

Chronic fatigue syndrome is a modern syndrome (identified less than a decade ago) that covers a multitude of symptoms, including chronic fatigue, pain, weakness, sleep disorders and mood disturbances. In many cases the symptoms are severe, persistent and disabling and cause considerable personal, social and healthcare costs. There is no obvious medical disease or major psychiatric illness.

Management involves graded exercise therapy (GET) to combat deconditioning and cognitive behavioural therapy (CBT) using behavioural techniques to gradually and consistently increase activity, reduce avoidance behaviour and improve confidence and illness control.

Differential diagnosis: Polymyalgia rheumatica (PMR) occurs commonly in older women and presents as aching and morning stiffness in the proximal muscles. Multiple sclerosis presents mostly with unilateral optic neuritis or progressive weakness of the legs. Other features of demyelination may be seen.

In hypochondriasis, the person's preoccupation is with the fear that they have a physical disease. Reassurance is unhelpful in these cases and they require some form of CBT.

A 44-year-old man presents with rhinitis, asthma and tender subcutaneous nodules. Antibodies to ANCA-PR3 and ANCA-MPO are present in his blood and the eosinophil count is  $1.2 \times 10^9/l$  (normal range  $0.04-0.4 \times 10^9/l$ ). A chest X-ray shows patchy pneumonitis.

What is the most likely diagnosis?

A Wegener's granulomatosis

B Churg-Strauss syndrome

C Microscopic polyangiitis

D Polyarteritis nodosa

E Rheumatoid arthritis



A	Wegener's granulomatosis
B	Churg-Strauss syndrome
C	Microscopic polyangiitis
D	Polyarteritis nodosa
E	Rheumatoid arthritis

## Explanation

### ANCA antibodies

- + The clinical triad of rhinitis, asthma and eosinophilia along with antibodies to ANCA-PR3 and ANCA-MPO is highly suggestive of Churg-Strauss syndrome (where ANCA-PR3 = antineutrophil cytoplasmic antibody proteinase 3 and ANCA-MPO = antineutrophil cytoplasmic antibody myeloperoxidase).
- + Microscopic polyangiitis also involves the lungs and can result in recurrent haemoptysis. ANCA-PR3 and ANCA-MPO antibodies are present but eosinophilia is not seen.
- + Wegener's granulomatosis usually presents with rhinorrhoea, cough, haemoptysis and pleuritic pain. Eosinophilia does not occur in this condition.
- + Subcutaneous nodules are seen in rheumatoid arthritis. Peripheral intrapulmonary nodules may occur, which may become large and cavitate in pneumoconiosis (Caplan syndrome). ANCA antibodies are usually absent in this condition.
- + Polyarteritis nodosa is ANCA-negative and rarely involves the lungs.

A 27-year-old man presents with swelling and pain in the proximal interphalangeal joints of both hands. He tells you that his symptoms have persisted for many months but he has resisted seeing the doctor because he is worried about the possible diagnosis. Both hands show ulnar deviation with pitting of the nails and onycholysis.

What could be the cause of his condition?

- |   |                        |
|---|------------------------|
| A | Rheumatoid arthritis   |
| B | Gonococcal arthritis   |
| C | Psoriatic arthritis    |
| D | Reactive arthritis     |
| E | Dermatophyte infection |

- |   |                        |
|---|------------------------|
| A | Rheumatoid arthritis   |
| B | Gonococcal arthritis   |
| C | Psoriatic arthritis    |
| D | Reactive arthritis     |
| E | Dermatophyte infection |

## Explanation

### Psoriatic arthropathy

Psoriatic arthropathy can mimic rheumatoid arthritis clinically and may be distinguished only by the presence of scaly lesions on the skin or nail changes. Dermatophytic infections are limited to the skin, hair, nails and mucous membranes. Nail changes do not occur in reactive or gonococcal arthritis.

A 55-year-old man presents with bowed legs, low back pain and increasing deafness over the past 6 months. His father was similarly affected at 60 years of age and died of bone cancer.

Given the likely clinical diagnosis, what would be the most characteristic finding in a blood test?

A	Decreased serum calcium levels
B	Elevated serum phosphate
C	Elevated serum alkaline phosphatase
D	Elevated ESR
E	Decreased 1,25-dihydroxycholecalciferol



- |   |   |
|---|---|
| A | Decreased serum calcium levels          |
| B | Elevated serum phosphate                |
| C | Elevated serum alkaline phosphatase     |
| D | Elevated ESR                            |
| E | Decreased 1,25-dihydroxycholecalciferol |

## Explanation

### Paget's disease

This patient has Paget's disease, typified by the deformity, deafness and positive family history. Serum calcium, phosphate and 1,25-dihydroxycholecalciferol levels are usually normal in this condition. The serum alkaline phosphatase is increased (it may exceed 1000 U/l) and this reflects increased bone turnover.

A 73-year-old man complains of right leg pain of 2 years' duration. There is no history of falls or injury. In the past he has been admitted to hospital for cardiac failure and takes inhaled bronchodilators and steroids for chronic obstructive pulmonary disease. Examination shows a healthy elderly man with mild tenderness of his right leg only. Routine blood tests show normal serum calcium and phosphate levels with a markedly raised alkaline phosphatase level.

What is the most likely diagnosis?

- |   |   |
|---|---|
| A | Osteoarthritis of the hip                 |
| B | Bony metastasis from an occult malignancy |
| C | Multiple myeloma                          |
| D | Paget's disease                           |
| E | Osteomalacia                              |

# Explanation

## Paget's disease of the bone

- + Paget's disease of the bone is a disorder of bone remodelling. There is uncontrolled bone turnover with excessive resorption, followed by disordered osteoblastic activity, which leads to abundant new bone formation
- + It is common in Europe, where it affects 10% of adults by the age of 90 years.

## Clinical features

- + The femur, pelvis, tibia, skull and lumbosacral spine are commonly involved
- + It presents with bony pain, deafness due to nerve compression/loss of cochlear BMD, high-output cardiac failure and deformities
- + The serum alkaline phosphatase level is markedly raised, with normal calcium and phosphate levels
- + Treatment is indicated for the bone pain and can range from simple analgesics to diphosphonates and calcitonin

A 68-year-old woman complained of pain at the base of her right thumb. There is no history of recent injury, or of any particular activities involving repeated movement of the joint. There was tenderness and swelling of the right first carpometacarpal joint.

What is the most likely diagnosis?

A    Avascular necrosis of the scaphoid

B    De Quervain's tenosynovitis

C    Osteoarthritis

D    Psoriatic arthritis

E    Rheumatoid arthritis



# Explanation

## Osteoarthritis

Osteoarthritis (OA) commonly affects the first carpometacarpal joint. Other commonly affected joints include the shoulders, hips, medial compartment of the knee and the proximal bones of the feet. Rheumatoid or seronegative arthritides tend to follow a more distal, symmetrical distribution.

## Management

The management of OA depends on which joints are affected, but pain relief is the mainstay of therapy. Non-steroidal anti-inflammatory drugs (NSAIDs) were previously widely used in the management of OA-associated pain, but recent scares about cardiac side-effects have resulted in a swing back to the use of simple pain relief. In lower-limb OA, weight reduction is advised, with joint replacement of the hip or knee in severe arthritis.

## Other notes

De Quervain disease is caused by stenosing tenosynovitis of the first dorsal compartment of the wrist. The first dorsal compartment at the wrist includes the tendons of the abductor pollicis longus. Patients with this condition usually report pain at the dorsolateral aspect of the wrist with referral of pain toward the thumb and/or lateral forearm. There is often a history of repetitive movement of the affected part (eg knitting, golf, lifting a baby). In De Quervain's radiographic changes are absent.

A 62-year-old man with a history of rheumatoid arthritis comes to the Respiratory Clinic for review. Over the past 4 months he has been losing weight and has developed a persistent cough, occasionally productive of blood stained sputum. Other past history of note includes hypertension for which they are treated with Lisinopril and Indapamide, and asthma which is managed with a low dose seretide inhaler. Examination reveals a BP of 142/82 mmHg, pulse is 80/min and regular. There are signs of right upper lobe consolidation. Temperature is 37.5°C.

Investigations:

Hb	10.9 g/dl
WCC	10.4 x10 <sup>9</sup> /l
PLT	181 x10 <sup>9</sup> /l
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	110 micromol/l
Quantiferon gamma test	positive
CXR	right upper lobe consolidation

Which of the following is the most likely cause?

A Azathioprine

B Infliximab

C Methotrexate

D Rituximab

E Tocilizumab



# Explanation

The answer is Infliximab -

Anti-TNF therapies are associated with increased risk of tuberculosis, the diagnosis here. For this reason patients should be evaluated for tuberculosis including risk of coming into contact with active TB before starting therapy. Azathioprine is associated with increased risk of neutropaenia in conjunction with xanthine oxidase inhibitors because of accumulation of 6-mercaptopurine. Rituximab is an anti-CD20 monoclonal antibody associated with B cell suppression and can therefore lead to increased risk of common bacterial infections. Tocilizumab is an anti-IL6 monoclonal, again associated with increased risk of common infections.

<http://www.medicines.org.uk/emc/medicine/3236/SPC/Remicade+100mg+powder+for+concentrate+for+solution+for+infusion/>



A 65-year-old white male, who is a chronic smoker, presents with low back and hip pain. His serum alkaline phosphatase level is 1000 IU/l, calcium 2.25 mmol/l and phosphate 1.2 mmol/l. Other liver function tests are normal. He also complains of difficulty in hearing.

What is the probable diagnosis?

A Squamous-cell carcinoma of the lung

B Multiple myeloma

C Osteomalacia

D Osteoporosis

E Paget's disease of bone

A 65-year-old man complains of progressive breathlessness, swelling of his ankles, painful joints and earache. An X-ray of his chest shows multiple nodules scattered throughout both lung fields. Urinalysis reveals proteinuria and microscopic haematuria.

What is the most probable diagnosis?

- |   |                              |
|---|------------------------------|
| A | Goodpasture's syndrome       |
| B | Berger's disease             |
| C | Wegener's granulomatosis     |
| D | Churg-Strauss syndrome       |
| E | Systemic lupus erythematosus |

# Explanation

## Wegener's granulomatosis

Wegener's granulomatosis is a potentially fatal disease caused by a generalised vasculitis that has a predisposition for the upper respiratory tract, lungs and kidneys. There can be nasal ulceration, rhinitis, otitis media, pulmonary symptoms and variable shadows on the chest X-ray (particularly multiple nodules), hypertension and glomerulonephritis.

### Differential diagnosis

- + Goodpasture syndrome is a proliferative glomerulonephritis with lung symptoms (haemoptysis). Arthritis and otitis media are not features of this condition.
- + Berger's disease is an IgA nephropathy that causes repeated episodes of glomerulonephritis and haematuria associated with viral infections. Pulmonary symptoms, arthralgia and otitis media do not occur in this condition.
- + Pulmonary infiltrates and asthma occur in vasculitis due to polyarteritis nodosa (PAN).
- + Churg-Strauss syndrome is vasculitis with significant pulmonary involvement and features that may be consistent with severe asthma.
- + Systemic lupus erythematosus (SLE) is a non-organ-specific autoimmune disease characterised by antinuclear antibodies and vasculitis. It is nine times more common in women and the onset is usually between 15 and 25 years of age. Conjunctivitis may occur in SLE. Nearly half the patients have pulmonary involvement (pleurisy with pleural effusion, restriction of lung volume).



A 70-year-old woman presented complaining of pain in her legs. A dual-energy X-ray absorptiometry (DEXA) scan revealed osteoporosis. Her doctor prescribed 400 IU of vitamin D along with calcium supplements.

Which is the most active metabolite of vitamin D involved in calcium homeostasis?

A	25-Hydroxycholecalciferol
B	7-Dehydrocholesterol
C	1,25-Dihydroxycholecalciferol
D	24,25-dihydroxycholecalciferol
E	Cholecalciferol



- |   |                                |
|---|--------------------------------|
| A | 25-Hydroxycholecalciferol      |
| B | 7-Dehydrocholesterol           |
| C | 1,25-Dihydroxycholecalciferol  |
| D | 24,25-dihydroxycholecalciferol |
| E | Cholecalciferol                |

## Explanation

### Vitamin D

The primary source of vitamin D in humans is photoactivation (in the skin) of 7-dehydrocholesterol to cholecalciferol. This is converted in the liver to 25-hydroxycholecalciferol and further converted by the kidney tubule enzyme  $1\alpha$ -hydroxylase to the active metabolite 1,25-dihydroxycholecalciferol. A less active metabolite (24,25-dihydroxycholecalciferol) is formed if vitamin D supplies are adequate.

An obese 50-year-old man presents in the middle of the night to the Emergency Department with swelling of his first metatarsophalangeal joint and left knee. On examination the joints are swollen, red, hot and tender.

Which examination would definitively confirm the suspected diagnosis?

A	ESR
B	Serum uric acid
C	Rheumatoid factor
D	Muscle biopsy
E	Examination of joint fluid

A	ESR
B	Serum uric acid
C	Rheumatoid factor
D	Muscle biopsy
E	Examination of joint fluid

## Explanation

### Diagnosis of gout

Definitive confirmation of gout requires the demonstration of monosodium urate monohydrate crystals by compensated polarised light microscopy of fluid from a gouty joint, bursa or tophus. Synovial fluid in acute attacks is typically turbid, with diminished viscosity and a greatly elevated cell count (more than 90% neutrophils). Chronic gouty fluid is more variable, but occasionally appears white due to the high crystal load.

A 39-year-old woman has been recently been diagnosed with systemic lupus erythematosus. She wants to know more about the possible symptoms that she may experience in the future.

What is the most common gastrointestinal complication seen in this condition?

A Autoimmune hepatitis

B Mesenteric vasculitis

C Pancreatitis

D Mouth ulcers

E Intestinal infarction



A	Autoimmune hepatitis
B	Mesenteric vasculitis
C	Pancreatitis
D	Mouth ulcers
E	Intestinal infarction

## Explanation

### Gastrointestinal involvement in SLE

Mouth ulcers are the most common gastrointestinal problem in systemic lupus erythematosus (SLE) and may be a presenting feature. Mesenteric vasculitis is more common in polyarteritis nodosa. Liver involvement is unusual, though lupoid antibodies have been noted in patients with autoimmune hepatitis. Pancreatitis is rare.

A 5-year-old Asian boy, who has been having episodes of fever and a persistent cough for the past 3 weeks, now complains of right hip pain. Blood tests show: white cell count (WCC)  $19 \times 10^9/l$ , erythrocyte sedimentation rate (ESR) 110 mm in 1st hour and C-reactive protein (CRP) 102 mg/l. An X-ray of the hip joint shows diffuse rarefaction.

What is the most likely diagnosis?

A	Septic arthritis
B	Tuberculous arthritis
C	Osteomyelitis
D	Reactive arthritis
E	Juvenile rheumatoid arthritis

# Explanation

## Tuberculous arthritis

The history and investigations are suggestive of tuberculous arthritis. Tuberculous arthritis usually affects children aged 2-5 years. The hip is one of the most frequently affected joints. Early X-ray signs are rarefaction of bone. Subsequently there is fuzziness of the joint margins and narrowing of the joint spaces. The white cell count, erythrocyte sedimentation rate and C-reactive protein levels are usually high.

## Differential diagnosis

- + Pyogenic arthritis of the hip is uncommon. A hot, painful, swollen joint usually accompanies this condition. Early X-rays are usually normal.
- + The distal femur or upper tibia is the common site for osteomyelitis. X-ray changes are not apparent for a few days but then show haziness and loss of density of the affected bone followed by subperiosteal reaction and, later, sequestrum and involucrum.
- + Reactive arthritis usually affects young adults and follows 4-6 weeks after genitourinary (chlamydial) or gastrointestinal (Shigella, Yersinia) infection. X-rays may show puffy periostitis at ligamentous insertions in the initial stages.
- + Still's disease (juvenile rheumatoid arthritis) occurs chiefly in prepubertal girls with mono- or polyarticular synovitis with erosion of cartilage, often preceded by fevers, iridocyclitis, pneumonitis, lymphadenopathy and splenomegaly. Early X-rays are usually normal in Still's disease.



A 40-year-old man presents with cough and haemoptysis. On examination he is found to have a nasal mucosal ulceration. The doctor suspects that this patient may be suffering from Wegener's granulomatosis.

Which tissues are most commonly involved in this condition?

A	Kidneys
B	Muscles
C	Respiratory tract
D	Gastrointestinal tract
E	Skin



A	Kidneys
B	Muscles
C	Respiratory tract
D	Gastrointestinal tract
E	Skin

## Explanation

### Wegener's granulomatosis

Wegener's granulomatosis characteristically affects the upper respiratory tract and lungs in 90% of cases. The disease usually starts with rhinorrhoea, with subsequent nasal mucosal ulceration, followed by cough, haemoptysis and pleuritic pain. The kidneys are affected in 80% of cases, musculoskeletal system in 60% and the gastrointestinal tract in 50%. Skin lesions are less common (40%).

Which one of the following pathological features is pathognomonic of the disease listed with below?

- A Reed-Sternberg cells in Hodgkin's disease
- B Cortical Lewy bodies (alpha-synuclein inclusions) in Lewy body dementia
- C Charcot-Leyden crystals in sputum from patient with asthma
- D Alcoholic hyaline (Mallory body) from liver biopsy specimen in alcoholic liver disease
- E Non-caseating granuloma in sarcoidosis

A Reed-Sternberg cells in Hodgkin's disease

B Cortical Lewy bodies (alpha-synuclein inclusions) in Lewy body dementia

C Charcot-Leyden crystals in sputum from patient with asthma

D Alcoholic hyaline (Mallory body) from liver biopsy specimen in alcoholic liver disease

E Non-caseating granuloma in sarcoidosis



# Explanation

## Pathognomonic features of diseases

A pathognomonic feature is a symptom or sign that is unique to a particular disease. The presence of such a sign or symptom allows positive diagnosis of the disease.

- + Although the histological diagnosis of Hodgkin's disease requires the presence of Reed-Sternberg cells, these cells are not pathognomonic of the disease and have been described in infectious mononucleosis and in other viral infections and malignancies.
- + The presence of alpha-synuclein inclusion bodies within cortical neurones is considered pathognomonic of Lewy Body Dementia; the same inclusion bodies are present in brainstem structures in Parkinson's disease.
- + Charcot-Leyden crystals (CLCs) have been found in many conditions associated with eosinophilia. Crystals of CLC protein in body fluids and secretions have long been considered a hallmark of eosinophil-associated allergic inflammatory diseases such as asthma, allergic rhinitis and also atopic dermatitis.
- + Alcoholic hyaline (Mallory body) is not specific for alcoholic liver disease because it has been detected in the livers of patients with Wilson's disease, primary biliary cirrhosis, hepatic carcinoma and following jejunio-ileal bypass.
- + The presence of non-caseating granuloma should not be construed as diagnostic of sarcoidosis until a thorough investigation of other causes of granulomatous inflammations has been conducted.



A 55-year-old woman known to suffer from severe disabling rheumatoid arthritis has a 12-month history of dyspnoea. She has also had a dry cough for that time. She has never smoked and has never been employed. Examination shows a woman of average build with severe hand deformities and nodules at the elbow. Cardiovascular examination is normal. Respiratory examination reveals a diffuse expiratory wheeze. Routine blood tests, a chest X-ray and an electrocardiogram (ECG) are all normal.

What is the most likely reason for her symptoms?

- |   |                                       |
|---|---------------------------------------|
| A | Bronchiolitis obliterans              |
| B | Chronic obstructive pulmonary disease |
| C | Bronchiectasis                        |
| D | Asthma                                |
| E | Pleural effusion                      |

A	Bronchiolitis obliterans
B	Chronic obstructive pulmonary disease
C	Bronchiectasis
D	Asthma
E	Pleural effusion

Explanation

# Explanation

## The lung in rheumatoid arthritis

Rheumatoid arthritis (RA) can affect the lungs in many ways. It is associated with:

- + Bronchiectasis
- + Pleural effusions
- + Lung nodules
- + Interstitial fibrosis
- + Bronchiolitis obliterans
- + Caplan syndrome

### Bronchiolitis obliterans

Bronchiolitis obliterans presents with a non-productive cough and dyspnoea. Physical examination might reveal a diffuse wheeze. The chest X-ray can be normal or can show a miliary or diffuse nodular pattern. Histology will show intraluminal polyps of organising connective tissue. It is treated with corticosteroids, but the prognosis is poor.

Other causes of bronchiolitis obliterans are: toxic fume inhalation, bone marrow transplantation, post-lung or post-heart transplantation, infections (viral and *Mycoplasma* and *Legionella* spp.), penicillamine, systemic lupus erythematosus (SLE) and polymyositis.

A 24-year-old man suddenly develops severe back pain while lifting some luggage. He is unable to straighten up and subsequently develops numbness and weakness in his left leg, followed by retention of urine. He is admitted to the Emergency Department where he is unable to move off the bed due to pain. Urinary retention is confirmed, as is motor and sensory loss affecting his left lower limb, and evidence of perianal sensory loss.

Given the likely clinical diagnosis, which plan of management is likely to be required?

- |   |                        |
|---|------------------------|
| A | Lumbar traction        |
| B | NSAIDs                 |
| C | Extension exercises    |
| D | Bedrest                |
| E | Laminectomy and fusion |



- |   |                        |
|---|------------------------|
| A | Lumbar traction        |
| B | NSAIDs                 |
| C | Extension exercises    |
| D | Bedrest                |
| E | Laminectomy and fusion |

## Explanation

### Cauda equina syndrome

This patient has features of cauda equina syndrome, presumably due to acute lumbar disc prolapse. This is an acute neurosurgical emergency. Alternating or bilateral sciatica with accompanying sensory symptoms and weakness in the lower limbs and feet and urinary retention suggest the diagnosis. Unless urgent neurosurgical assessment and treatment is initiated, chronic neurological damage may result.

A 32-year-old woman presents with left inguinal and groin pain of 1 week's duration that is worse with weight bearing and ambulation. Physical examination reveals a full range of motion of the left hip. She walks with a limp. She has previously been treated with aggressive chemotherapy for Hodgkin's disease. An anteroposterior film of the pelvis demonstrates no osseous abnormality.

Which one of the following tests would be most useful in making the diagnosis?

- |   |  |
|---|--|
| A | Serum rheumatoid factor                    |
| B | Erythrocyte sedimentation rate             |
| C | Magnetic resonance imaging of the left hip |
| D | Arthrogram of the left hip                 |
| E | Blood alcohol level                        |

C	Magnetic resonance imaging of the left hip
D	Arthrogram of the left hip
E	Blood alcohol level

## Explanation

### Osteonecrosis

Osteonecrosis (avascular necrosis) is one of the most common causes of hip pain and incapacity in patients with a variety of diseases who have been treated with corticosteroids.

### Diagnosis

A major problem in diagnosing osteonecrosis relates to the lag between the onset of symptoms (pain and limp) and the appearance of defined radiographic changes. Magnetic resonance imaging has been shown to be extremely valuable in evaluating high-risk patients who are symptomatic but radiographically normal.

### Risk factors

Apart from corticosteroid use, other risk factors for avascular necrosis include prolonged heparin treatment, exposure to high barometric pressures (diving), excessive alcohol intake and sickle cell disease.



A 54-year-old Italian woman presents with purpura, pain in both knee joints and Raynaud's phenomenon. Urinalysis shows proteinuria and haematuria. A biopsy of the right kidney shows large, amorphous, periodic acid-Schiff- (PAS-) positive, Congo red-negative deposits within glomerular capillary lumens. Electron microscopy shows an amorphous or fibrillar appearance.

Given the likely diagnosis, which organ or tissue is most commonly involved in this condition?

- |   |                        |
|---|------------------------|
| A | Skin                   |
| B | Musculoskeletal system |
| C | Kidneys                |
| D | Nervous system         |
| E | Gastrointestinal tract |



A

Skin

B

Musculoskeletal system

C

Kidneys

D

Nervous system

E

Gastrointestinal tract

## Explanation

### Cryoglobulinaemia

This patient most probably has cryoglobulinaemia. Cryoglobulins are immunoglobulins that precipitate reversibly in the cold.

#### Clinical features

- + There is skin involvement in over 90%, with purpura, leg ulcers and Raynaud's phenomenon.
- + Arthralgia is seen in 70%.
- + Glomerular disease is common in types 2 and 3 (mixed types) and occurs in around 50-55% of cases.
- + Neurological involvement (polyneuropathy) is seen in 40% of patients.
- + The gastrointestinal tract is affected in 30%.

An obese 50-year-old man presents in the middle of the night to the Emergency Department with swelling of his first metatarsophalangeal joint and left knee. On examination the joints are swollen, red, hot and tender.

Given the likely diagnosis, what is the most appropriate treatment?

A	Steroids
B	Indometacin
C	Erythromycin
D	Ampicillin
E	Methotrexate

A	Steroids
B	Indometacin
C	Erythromycin
D	Ampicillin
E	Methotrexate

## Explanation

### Treatment of gout

This patient clearly has gout, a condition well associated with obesity and recognised as a feature of the metabolic syndrome. Rapid symptom relief from gout may be obtained with a quick-acting non-steroidal anti-inflammatory drug (NSAID), given in full dosage. Although indometacin has a long tradition in this context, it should be carefully chosen for use in the elderly because of its frequent renal, gut and nervous system side-effects. Long term therapy would be with allopurinol.



A 44-year-old man complaining of bone and joint pains is found to have osteopenia. His doctor feels that his present condition may be due to the lack of attainment of peak bone mass at around 30 years of age.

What is the most important influence on peak bone mass attainment in an individual?

A	Vitamin D deficiency
B	Sex hormone status
C	Physical activity
D	Calcium deficiency
E	Genetic factors

A	Vitamin D deficiency
B	Sex hormone status
C	Physical activity
D	Calcium deficiency
E	Genetic factors

## Explanation

### Peak bone mass

Genetic factors are the single most significant influencing factor for peak bone mass. Studies including the Hertfordshire Cohort Study suggest that birth weight is closely correlated to risk of osteoporosis, and body morphology including fat mass have a strong genetic component. After a peak at around 30 years of age there is a gradual decline in bone mass in men. In contrast, accelerated loss occurs in the 10 years following the menopause in women.

A 22-year-old homosexual man gives a history of high-grade fever associated with pustules on his hands and severe joint pain 4 weeks ago. His left knee is now swollen and red. Cultures from blood and joint aspirate are negative. Urethral discharge shows the presence of gonococci. He has a history of penicillin sensitivity.

Which drug would be most suitable in this condition?

A	Oral penicillin
B	Amoxicillin
C	Prednisolone
D	Azithromycin
E	Ciprofloxacin

A	Oral penicillin
B	Amoxicillin
C	Prednisolone
D	Azithromycin
E	Ciprofloxacin

## Explanation

### Treatment of gonococcal arthritis

This patient has gonococcal arthritis. First line therapy would usually be IV Ceftriaxone, given it is not listed here, Azithromycin is the first choice from the options we are given. Whilst gonococcus was historically sensitive to quinolones, there is now significant resistance.



A 26-year-old man presents to the Emergency Department with pain affecting his left knee, right ankle and both heels. He has also suffered from conjunctivitis over the past few days and some burning and stinging whilst passing urine. He returned from a holiday with friends in Spain a few days earlier, during which he admits to having unprotected sex with a number of female partners. His BP is 105/80 mmHg, pulse is 85/min and regular, his temperature is 38.0°C. You note a psoriasis-like rash affecting both feet. There is evidence of active synovitis affecting the knee, ankle and heels. Investigations reveal a raised ESR and a mild leukocytosis, and urethral swab is positive for chlamydia.

Which of the following is the most appropriate intervention for his joint pains?

A	Doxycycline
B	Naproxen
C	Penicillin V
D	Prednisolone
E	Sulphasalazine

A	Doxycycline
B	Naproxen
C	Penicillin V
D	Prednisolone
E	Sulphasalazine

## Explanation

The answer is Naproxen -

Whilst this man requires antibiotic therapy for his chlamydial infection, intervention with antibiotics has not been shown to shorten the course of the reactive arthritis. NSAIDs should be used in the first instance to manage arthritis, with prednisolone the next option in patients who fail to respond to NSAIDs alone. Sulphasalazine is the most commonly used second line therapy in patients with reactive arthritis; Methotrexate and Ciclosporin are alternative potential options. Where the episode of reactive arthritis becomes prolonged, and features of lumbosacral spine involvement develop, anti-TNF agents may be of value.

A 43-year-old woman presents with dry mouth, dry eyes and bilateral parotid swelling. She also complains of itchy skin over the arms, legs and upper body and a dry cough. She has a history of mild hypertension for which she takes Amlodipine, but nil else of note. Examination reveals a BP of 135/70 mmHg, pulse is 70/min and regular. You confirm the bilateral parotid swelling.

Investigations;

Hb	13.2 g/dl
WCC	$9.4 \times 10^9/l$
PLT	$231 \times 10^9/l$
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	110 micromol/l
ESR	61 mm/1 <sup>st</sup> hour

Which of the following autoantibody tests, if positive, would be most suggestive of Sjögren's syndrome?

Which of the following autoantibody tests, if positive, would be most suggestive of Sjögren's syndrome?

- |   |                             |
|---|-----------------------------|
| A | Anti-SSB                    |
| B | Anti-nuclear antibody       |
| C | Anti-smooth muscle antibody |
| D | p-ANCA                      |
| E | c-ANCA                      |



# Explanation

The answer is Anti-SSB -

Anti-SSB and anti-SSA antibodies are each found in approximately 50% of individuals with Sjögren's syndrome. Whilst other antibodies such as ANA may be positive, they do not form part of the diagnostic criteria for Sjögren's.

According to the American-European classification system, diagnosis of primary Sjögren syndrome requires 4 of 6 of the below criteria; in addition, either criterion number 5 or criterion number 6 must be included. Sjögren syndrome can be diagnosed in patients who have no sicca symptoms if 3 of 4 objective criteria are fulfilled. The criteria are as follows:

1. Ocular symptoms - Dry eyes for more than 3 months, foreign-body sensation, use of tear substitutes more than 3 times daily
2. Oral symptoms - Feeling of dry mouth, recurrently swollen salivary glands, frequent use of liquids to aid swallowing
3. Ocular signs - Schirmer test performed without anesthesia ( $< 5$  mm in 5 min), positive vital dye staining results
4. Oral signs - Abnormal salivary scintigraphy findings, abnormal parotid sialography findings, abnormal sialometry findings (unstimulated salivary flow  $< 1.5$  mL in 15 min)
5. Positive minor salivary gland biopsy findings
6. Positive anti-SSA or anti-SSB antibody results

A 38-year-old man complains of increasing exertional dyspnoea. On examination, he has severe thoracic kyphosis. Fine inspiratory crepitations at the apices are heard on auscultation of the chest. X-ray of the spine shows ossification of the anterior longitudinal ligament and facet joint fusion. There is also significant calcification and arthritic changes around both SI joints.

What is the condition?

A	Ankylosing spondylitis
B	Reiter's syndrome
C	Fibrosing alveolitis
D	Scheuermann's disease
E	Rheumatic pulmonary nodules

## Explanation

Ankylosing spondylitis

The clinical picture and X-ray findings are characteristic of ankylosing spondylitis. Associated apical fibrosis of the lungs may occur in only 1% of cases, but respiratory problems due to severe kyphosis are common.



A 33-year-old woman comes to the Rheumatology Clinic complaining of weight loss and night sweats, with joint pains affecting her fingers, toes wrists and knees over the past 4 months. She has no significant past medical history apart from mild psoriasis affecting her scalp and long standing idiopathic epilepsy. Her only regular medications are the progesterone only pill and Lamotrigine. On examination her temperature is 37.6°C, BP is 149/88 mmHg; pulse is 82/min and regular. There are signs of small joint polyarthritis and an erythematous rash affecting her face.

Investigations;

Hb	10.4 g/dl
WCC	10.8 x10 <sup>9</sup> /l
PLT	161 x10 <sup>9</sup> /l
ESR	82 mm/1 <sup>st</sup> hour
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.9 mmol/l
Creatinine	132 micromol/l
Urine	blood ++, protein ++
Anti-nuclear antibody	positive
Rheumatoid factor	positive
Anti-CCP	negative
Anti-dsDNA	positive



Which of the following is the most likely diagnosis?

- |   |                                 |
|---|---------------------------------|
| A | Drug-induced lupus (DLE)        |
| B | Mixed connective tissue disease |
| C | Psoriatic arthritis             |
| D | Rheumatoid arthritis            |
| E | SLE                             |

## Explanation

The answer is SLE -

The clinical picture fits best with SLE, and the antibody picture supports this as the underlying diagnosis versus drug-induced lupus, which is more likely to be associated with anti-ssDNA antibodies. With regards to anti-epileptic drugs, DLE is more commonly seen in conjunction with Carbamazepine or Sodium valproate rather than Lamotrigine. Positive rheumatoid factor is a common finding in patients with SLE. The presence of haematuria and proteinuria and negative anti-CCP antibodies further support a diagnosis of SLE versus rheumatoid.

A 57-year-old woman presents with shortness of breath. She has trouble with Raynaud's phenomenon, for which she wears gloves all the time and takes amlodipine. She also has a history of reflux oesophagitis, for which she takes regular omeprazole. On examination she looks thin and tired, her body mass index (BMI) is  $18 \text{ kg/m}^2$  and her blood pressure is 162/89 mmHg. There is calcinosis on examination of the fingers. She has an elevated respiratory rate at rest. On auscultation you can hear crackles at both lung bases. Investigations show: haemoglobin 11.1 g/dl, white cell count  $7.9 \times 10^9/\text{l}$ , platelets  $187 \times 10^9/\text{l}$ , sodium 139 mmol/l, potassium 4.9 mmol/l, creatinine  $148 \mu\text{mol/l}$ .

Which one of the following investigations is likely to contribute most to the diagnosis of her underlying respiratory problem?

- A High resolution CT
- B CT pulmonary angiogram
- C CXR
- D Transfer factor
- E Pulmonary function tests

A	High resolution CT
B	CT pulmonary angiogram
C	CXR
D	Transfer factor
E	Pulmonary function tests

## Explanation

### Systemic sclerosis

The suspicion is that this patient has systemic sclerosis with symptoms of Raynaud's, oesophageal dysmotility and calcinosis on examination of the fingers. Her shortness of breath is therefore suggestive of the possibility of pulmonary fibrosis. The most accurate way to evaluate this is ultimately with high resolution computed tomography, and this would be the investigation of choice.



You are asked to see a 50-year-old man in the surgical ward at 6 am who underwent an uncomplicated cholecystectomy for gallstones the day before. He has developed excruciating pain in his right ankle joint. He has a history of angina and hypertension, for which he takes bendroflumethiazide (bendrofluazide) and aspirin. Examination of his cardiovascular and respiratory system is unremarkable, as is his abdomen. His right ankle is red, warm, swollen and tender. Routine blood tests show mildly impaired renal function.

What is the most likely diagnosis?

- |   |                      |
|---|----------------------|
| A | Cellulitis           |
| B | Deep vein thrombosis |
| C | Septic arthritis     |
| D | Gout                 |
| E | Rheumatoid arthritis |

# Explanation

## Gout

Gout is an abnormality of uric acid metabolism that results in the deposition of sodium urate crystals in joints, soft tissue and urinary tract. It is due to hyperuricaemia resulting from the overproduction or under-excretion of uric acid.

It mainly affects men and an acute attack usually begins suddenly in the early hours of the morning. Attacks may be precipitated by:

- + Surgical operations
- + Starvation
- + Dietary or alcoholic excess
- + Drugs (eg diuretics)

It usually attacks the big toe, but the ankle, knee or other toe joints can be affected in 25% of the patients. The joint is typically red, warm and tender. Aspirating the affected joint and examining the synovial fluid under polarised light microscopy will show long, needle-shaped, negatively birefringent crystals, which are diagnostic. A normal serum uric acid does not exclude the diagnosis of gout. Acute attacks should be treated with an anti-inflammatory drug.

A 72-year-old woman comes to see you because she finds taking her bisphosphonate tablets an inconvenience. She is concerned that her tablets, which seem rather large, should be taken whole, and swallowed with plenty of water while sitting or standing at least 30 minutes before breakfast (or any other oral medicine). This is rather inconvenient as she has diabetes. The patient should then sit or stand upright for 30 minutes after taking the tablet.

How would you explain the reason for this to her?

- A To shorten the time over which the medicine is absorbed
- B To reduce GI side-effects
- C To prevent interaction with other medications
- D Because of reduced gastric emptying
- E To reduce the incidence of osteonecrosis of the jaw

- |   |   |
|---|---|
| A | To shorten the time over which the medicine is absorbed |
| B | To reduce GI side-effects                               |
| C | To prevent interaction with other medications           |
| D | Because of reduced gastric emptying                     |
| E | To reduce the incidence of osteonecrosis of the jaw     |

## Explanation

### Bisphosphonates

All bisphosphonates are known to be associated with dysphagia, oesophagitis, and either oesophageal or gastric ulcers. For this reason patients are encouraged to stand up and drink plenty of water to allow the bisphosphonate to pass into the stomach. Additionally, milk may reduce bioavailability of bisphosphonates, so it is recommended that the medication be taken with water only. The speed of absorption of bisphosphonate does of course have no influence on the risk of osteonecrosis of the jaw.



A 25-year-old man complains of joint pain of 3 weeks' duration, mainly affecting the joints of his lower limbs. He also mentions that he has had low backache for the last 2 weeks. When he was on holiday in Spain 6 weeks ago, he had a mild gastrointestinal upset that settled spontaneously. He also mentioned that his eyes had been irritated, but that this had now settled, and that he underwent an appendicectomy 3 years ago. On examination he is pyrexial, with a temperature of 37.5 °C. Routine blood tests show a raised erythrocyte sedimentation rate (ESR) and a normal white cell count.

Which one of the following is true?

A	He needs high-dose corticosteroids
B	Rheumatoid factor is likely to be negative
C	Aspirated synovial fluid from an inflamed joint will clinch the diagnosis
D	X-rays of the affected joints are essential in making the diagnosis
E	A rash is commonly seen in such patients

- |   |   |
|---|---|
| A | He needs high-dose corticosteroids  |
| B | <b>Rheumatoid factor is likely to be negative</b>                         |
| C | Aspirated synovial fluid from an inflamed joint will clinch the diagnosis |
| D | X-rays of the affected joints are essential in making the diagnosis       |
| E | A rash is commonly seen in such patients                                  |

## Explanation

### Reactive arthritis

The history of joint pains following a gastrointestinal upset and irritation of the eyes (suggestive of conjunctivitis) suggests a diagnosis of reactive arthritis. This usually follows either a gastrointestinal infection or non-specific urethritis. It is characterised by seronegative arthritis, conjunctivitis and up to 10% of patients may develop keratoderma blennorrhagica (intense scaling of the skin on the sole of the feet). The diagnosis is clinical. Treatment is with anti-inflammatory drugs and there is a high incidence of recurrence.

A 72-year-old woman is admitted for elective knee replacement. She has a past history of hypertension which is controlled with Indapamide, but nil else of note. Her BMI is 25 and the procedure itself goes well with no complications.

Which of the following is the correct advice with respect to DVT prophylaxis?

- |   |   |
|---|---|
| A | Low molecular weight heparin started 24 hours after surgery |
| B | TED anti-embolism stockings only                            |
| C | Aspirin 75mg peri-surgery                                   |
| D | Dabigatran started 2 hours after surgery                    |
| E | Fondaparinux started 24 hours after surgery                 |

## Explanation

The answer is Dabigatran started 2 hours after surgery

Low molecular weight heparin, oral factor X inhibitors such as Dabigatran and s/c factor X inhibitors such as Fondaparinux are all recommended as potential options for DVT prophylaxis in elective knee replacement surgery. Low molecular weight heparin or Fondaparinux should be started 6-12 hours after surgery. In the case of oral factor X inhibitors, the recommendation is to start Dabigatran 1-4 hours after surgery, slightly later for Rivaroxaban.

<https://www.nice.org.uk/guidance/ta157/chapter/2-The-technology>



A 50-year-old woman with a 20-year history of rheumatoid arthritis in both hands suddenly develops finger drop of the ring finger of her right hand.

Which deformity is most likely to have caused this complication?

- |   |  |
|---|--|
| A | Fixed hyperextension (swan-neck deformity) of the proximal interphalangeal joint |
| B | Ulnar deviation at the metacarpophalangeal joints                                |
| C | Boutonnière deformity  |
| D | Swelling and dorsal subluxation of the ulnar styloid                             |
| E | Squared hand and fixed adduction of the thumb                                    |

- |   |  |
|---|--|
| A | Fixed hyperextension (swan-neck deformity) of the proximal interphalangeal joint |
| B | Ulnar deviation at the metacarpophalangeal joints                                |
| C | Boutonnière deformity  |
| D | Swelling and dorsal subluxation of the ulnar styloid                             |
| E | Squared hand and fixed adduction of the thumb                                    |

## Explanation

### Hand deformities in rheumatoid arthritis

Swelling and dorsal subluxation of the ulnar styloid leads to wrist pain and may cause rupture of the finger extensor tendons. This causes finger drop of the little and ring fingers predominantly, which needs urgent surgical repair. Swan-neck and Boutonnière deformities and ulnar deviation at the metacarpophalangeal joints occur in rheumatoid arthritis, but do not cause finger drop.

The squared hand is seen in severe nodal osteoarthritis and is caused by bony swelling of the carpometacarpal joint and fixed adduction of the thumb.

A 65-year-old man has a history of long-standing neck pain radiating to his arm, with increased neck pain, limitation of neck movement and inability to lift his right arm above the shoulder. An X-ray shows narrowing of the disc space between the C5 and C6 vertebrae.

What is the most likely diagnosis?

- |   |                            |
|---|----------------------------|
| A | Cervical spondylosis       |
| B | Prolapsed cervical disc    |
| C | Cervical spondylolisthesis |
| D | Spasmodic torticollis      |
| E | Cervical rib               |

## Explanation

### Prolapsed cervical disc

A prolapsed cervical disc most commonly affects the C5/C6 and C6/C7 vertebrae. Central protrusions can lead to symptoms of spinal cord compression. Posterolateral protrusions can cause a stiff neck, pain radiating to the arm, weakness of the muscles affected by the nerve root and depressed reflexes.

### Differential diagnosis

- + Cervical spondylosis occurs as a result of osteoarthritis. Disc spaces can be narrowed and osteophytes seen in the central and posterior intervertebral joints. Muscle weakness is uncommon.
- + Cervical spondylolisthesis is the spontaneous displacement of one vertebra upon another and can usually be seen on X-ray.
- + A cervical rib can present with similar symptoms but the X-ray would be diagnostic.
- + Sudden onset of a stiff painful neck with torticollis can occur in adults due to spasm of the trapezius and sternocleidomastoid muscles. X-ray of the cervical spine is usually normal in this condition.



A 31-year-old man with nephrotic syndrome complains of a 2-month history of pain in his right hip joint. The movements of the hip are free but painful. An X-ray provides evidence of a completely destroyed femoral head.

What is the most probable diagnosis?

- |   |   |
|---|---|
| A | Tuberculosis of the hip                   |
| B | Avascular necrosis of the femoral head    |
| C | Pathological fracture of the femoral neck |
| D | Septic arthritis                          |
| E | Gouty arthritis                           |

## Explanation

### Avascular necrosis of the femoral head

This patient is most probably on long-term steroid treatment. High doses of steroids can predispose to avascular necrosis of the femoral head. Initially, movements are restricted, particularly abduction and internal rotation. Subsequently the movements become free when the femoral head is completely destroyed. A pathological fracture would be evident on X-ray.

Tuberculosis of the hip would be unlikely in the absence of other symptoms of pain, joint swelling and fever. Septic arthritis would be much more acute in presentation, and movements would be limited, if not impossible, due to pain in the initial stages and ankylosis later on. Gout usually affects the small joints of the feet or hands. There is no association with nephrotic syndrome or its management.

A 70-year-old woman presents with pain over her left hip, which occurred suddenly with no history of trauma. Past history of note includes severe chronic obstructive pulmonary disease (COPD), for which she is managed with multiple medications, including combination steroid and long-acting  $\beta$ -agonist inhaler and chronically prescribed oral corticosteroids.

On examination she looks cushingoid in appearance, there is pain over the hip and clicking on movement. Flexion, abduction and internal rotation are limited and she walks with a marked limp. You suspect that she may have avascular necrosis of the hip.

Which one of the following is the most sensitive examination to support early diagnosis?

A	MRI
B	Ultrasound
C	X-ray
D	CT scan
E	Bone scan

A	MRI
B	Ultrasound
C	X-ray
D	CT scan
E	Bone scan

## Explanation

### Diagnosis of avascular necrosis of the hip

- + This patient is cushingoid and has sudden onset pain over her left hip. Without a history of trauma this raises the possibility of avascular necrosis (AVN) of the hip.

### Bone scanning in AVN

- + During the early stages of avascular necrosis of the hip, a bone scan is particularly sensitive at detecting the abnormality.
- + Whilst changes can be seen early on radionuclide scanning, it is MRI that is seen as the investigation of choice, with a sensitivity that exceeds 90%.



A 12-year-old girl complains of pain in her hip and knee joints, as well as fever, bloody diarrhoea and abdominal pain. A barium enema shows rose-thorn ulcers.

What is the most characteristic feature seen on colonoscopy in this condition?

A Red-raw mucosa

B Pseudopolyps

C Discrete ulcers

D Colonic dilatation

E Diverticula

A	Red-raw mucosa
B	Pseudopolyps
C	Discrete ulcers
D	Colonic dilatation
E	Diverticula

## Explanation

### Enteropathic arthritis

Both Crohn's disease and ulcerative colitis may be associated with enteropathic arthritis. Barium studies in Crohn's disease may show strictures, rose-thorn ulcers and cobblestone mucosal surfaces. Colonoscopy may show discrete ulcers. Red-raw mucosa, pseudopolyps and evidence of colonic dilatation are features of ulcerative colitis. Diverticular disease does not present with arthralgia.

A 67-year-old man known to be hypothyroid says he woke up in the morning with a painful, warm, red and swollen right knee. An X-ray of his knee shows calcification of the meniscus only.

What is the most likely diagnosis?

- |   |                           |
|---|---------------------------|
| A | Acute gout                |
| B | Osteoarthritis            |
| C | Rheumatoid arthritis      |
| D | Pyrophosphate arthropathy |
| E | Septic arthritis          |

## Explanation

### Pyrophosphate arthropathy

Pyrophosphate arthropathy is characterised by the deposition of calcium pyrophosphate dihydrate (CPPD) crystals in fibrous and articular cartilage. Shedding of crystals into the joint spaces provokes an attack of pseudogout.

This may present clinically as a sudden onset of pain, inflammation and swelling of the knee. Radiography may show calcification of the articular cartilage or menisci. Examination of the synovial fluid under polarising light microscopy allows the identification of CPPD crystals. Hypothyroidism, hyperparathyroidism, hypomagnesaemia, haemochromatosis and hypophosphatasia are some of the metabolic disorders that predispose to pyrophosphate arthropathy



A 66-year-old man presents complaining of acute loss of vision in his right eye with a history of right-sided headache for the past 4 months. He also has pain in his jaw while eating. Fundoscopy reveals a swollen optic disc with flame-shaped haemorrhages. Eye movements are painless. Investigations reveal a raised erythrocyte sedimentation rate (ESR). A temporal artery biopsy is reported as normal.

What is the most likely cause of his condition?

- |   |                                |
|---|--------------------------------|
| A | Diabetic retinopathy           |
| B | Giant-cell arteritis           |
| C | Polyarteritis nodosa           |
| D | Sjögren syndrome               |
| E | Central retinal vein occlusion |

# Explanation

## Giant-cell arteritis

Giant-cell arteritis is a large-vessel vasculitis predominantly affecting branches of the temporal and ophthalmic arteries. The mean age of onset is 70 years, with a female to male ratio of 4:1.

The most important clinical features are headache localised to the temporal or occipital region with scalp tenderness, jaw pain due to ischaemia of the masseters and visual disturbance due to vasculitis of the posterior ciliary artery, which supplies the optic nerve. This causes acute anterior ischaemic optic neuropathy. Damage to the optic nerve results in loss of visual acuity and field, reduced colour perception and pupillary defects. Investigations: the erythrocyte sedimentation rate (ESR) is usually elevated above 50 mm in 1st hour; skip lesions are common, and a negative biopsy does not exclude the diagnosis.

## Differential diagnosis

Diabetic retinopathy is the most common cause of blindness in adults between 30 and 65 years of age in developed countries. Features include microaneurysms, retinal haemorrhages, exudates, cotton-wool spots, venous changes and neovascularisation.

Classic polyarteritis nodosa (PAN) is a necrotising vasculitis. All age groups can be affected. Hepatitis B is a risk factor. The characteristic presentation is with myalgia, arthralgia, fever and weight loss. Ocular involvement is rare.

Sjögren syndrome is an autoimmune disorder of unknown aetiology characterised by lymphocytic infiltration of salivary and lacrimal glands.

Central retinal vein occlusion can occur in chronic simple glaucoma, arteriosclerosis, hypertension and polycythaemia. The fundus is like a 'stormy sunset' (red haemorrhagic areas with engorged veins).

You review a 48-year-old woman who presents complaining of joint pains and who has suffered recurrent infections over the past few months. She has a positive rheumatoid factor on blood testing and a low white cell count.

Given the likely diagnosis, which one of the following features is most likely to be found in her case?

A	Splenic atrophy
B	Splenomegaly
C	Distal interphalangeal joint involvement
D	Flexural surface rheumatoid nodules
E	HLA-DR2 tissue type



- |   |  |
|---|--|
| A | Splenic atrophy                          |
| B | <b>Splenomegaly</b>                      |
| C | Distal interphalangeal joint involvement |
| D | Flexural surface rheumatoid nodules      |
| E | HLA-DR2 tissue type                      |

## Explanation

### Felty syndrome

Felty syndrome is associated with rheumatoid arthritis and consists of splenomegaly and neutropenia in a patient with rheumatoid arthritis. Leg ulcers or sepsis are associated complications. There is an association with HLA-DR4.

The hands are commonly involved in rheumatoid arthritis, but it is more usual for the proximal interphalangeal joints to be involved. Rheumatoid nodules are found in a high percentage of patients and occur most commonly on the extensor surfaces of joints such as the elbows.



A 42-year-old woman presents with low-grade fever, fatigue and weight loss. In addition she has suffered from increasing headaches and joint pains over the past few months. She has no significant past medical history of note. On examination she is mildly hypertensive at 148/90 mmHg and has a body mass index (BMI) of 21 kg/m<sup>2</sup>. She has a malar rash affecting her face. There are signs of symmetrical joint tenderness affecting her wrists, knees, metacarpophalangeal and PCP joints on both sides.

Investigations show: haemoglobin 10.9 g/dl, white cell count  $8.2 \times 10^9/l$ , platelets  $82 \times 10^9/l$ , erythrocyte sedimentation rate (ESR) 56 mm in 1st hour, sodium 140 mmol/l, potassium 4.9 mmol/l, creatinine 134  $\mu\text{mol/l}$ .

What threshold for antinuclear antibody titre is the threshold for considering systemic lupus erythematosus (SLE) as the underlying diagnosis?

A	1:10
B	1:20
C	1:40
D	1:400
E	1:160

D	1:400
E	1:160

## Explanation

### Antinuclear antibodies

- + A low titre of antinuclear antibodies may be present in individuals who are completely well
- + Hence, dilutions given here (of 1:100 or less) in terms of dilution would not prompt you to consider lupus as the cause
- + Up to 20% of the population aged over 50 years have a titre between 1:40 and 1:400, so the test should only be requested if underlying connective tissue disease is suspected
- + In the presence of symptoms a titre of 1:160 or greater would be considered significant and suspicious of a diagnosis of lupus
- + In summary the greater the dilution at which a reaction is detected, the more chance a patient has of having SLE
- + Further elucidation of the pattern of immunophoresence, such as looking for a homogeneous staining pattern, may help to confirm a diagnosis of systemic lupus erythematosus versus other connective tissue disorders.

Your review a 62-year-old woman with osteoarthritis.

Which one of the following stems is true of osteoarthritis?

- |   |   |
|---|---|
| A | Defects in collagen Type I genes in familial osteoarthritis (OA) of the hips and knees  |
| B | Defects in collagen Type II genes in familial osteoarthritis (OA) of the hips and knees |
| C | Commonly distal polyarticular joint involvement   |
| D | Raised ESR  |
| E | Mild hip dysplasia is not associated with future osteoarthritis (OA) of the hip         |



A	Defects in collagen Type I genes in familial osteoarthritis (OA) of the hips and knees
B	Defects in collagen Type II genes in familial osteoarthritis (OA) of the hips and knees
C	Commonly distal polyarticular joint involvement
D	Raised ESR
E	Mild hip dysplasia is not associated with future osteoarthritis (OA) of the hip

## Explanation

### Osteoarthritis

Osteoarthritis (OA) is a disease of synovial joints characterised by cartilage loss and accompanying periarticular bone response. The incidence increases with age and it is most common in the over-60s. Familial osteoarthritis may be associated with mutations in collagen type II genes. There are a few predisposing conditions, including farming (OA hip), cotton workers (OA of the hand) and mild hip dysplasia (OA of the hip). Management involves weight reduction in overweight or obese people with large-joint arthritis and adequate pain relief.

### Pathological changes in the bone

It is thought that cartilage becomes oedematous early in the development of OA and this is followed by the development of focal areas of erosion. This then leads to death of chondrocytes and a fibrillated and fissured cartilaginous surface. Eventually ulceration leads to exposure and stress on underlying bone. Bony repair is attempted, overgrowth occurs and osteophytes form.



A 25-year-old woman presents with a small joint polyarthropathy has significantly affected her work as an artist over the last 6 months. Her pain is worst in her fingers, elbows and wrists. She has also felt increasing lethargy and has lost 2kg in weight over the past 6 weeks. Physical examination confirms evidence of active synovitis bilaterally.

Which of the following tests is most useful in confirming a diagnosis of rheumatoid arthritis?

A	Anti-CCP antibody
B	Anti-nuclear antibody
C	Bilateral hand x-ray
D	ESR
E	Ferritin

## Explanation

The answer is Anti-CCP antibody

Whilst rheumatoid factor is the traditional antibody test for RA, it is only positive in 60-70% of individuals with the disease, anti-CCP is a reasonable alternative as it is more specific than rheumatoid factor and predictive of progression to erosive joint disease. Anti-nuclear antibodies are associated with SLE. ESR and ferritin are non-specific markers of inflammation. X-ray changes occur later in the disease and are not therefore useful with respect to early intervention.

A 50-year-old obese patient presents in the middle of the night to the Emergency Department with swelling of his first metatarsophalangeal joint and left knee. On examination the joints are swollen, red, hot and tender.

What is the most likely diagnosis?

- |   |                      |
|---|----------------------|
| A | Osteoarthritis       |
| B | Gout                 |
| C | Rheumatoid arthritis |
| D | Osteomyelitis        |
| E | Dermatomyositis      |

# Explanation

## Gout

In almost all initial episodes of gout a single peripheral joint is involved. This is the first metatarsophalangeal joint ('podagra') in 50% of first attacks and in 70% of all attacks. Other common sites are the knees, ankles, mid-tarsal joints, small hand joints, wrists and elbows. The axial skeleton and large central joints are rarely involved, and never as the first site.

## Clinical features

Attacks often wake the patient in the early morning with localised irritation and aching. Within a few hours the joint and surrounding tissues are swollen, hot, red, shiny and extremely painful. The patient cannot bear even bedclothes to touch the joint, and it is often described as the worst pain ever experienced. Inflammation is maximal within 24 hours and is often associated with pyrexia and malaise. Examination reveals florid synovitis and swelling, extreme tenderness and overlying erythema. If left untreated, the attack resolves spontaneously over 5-15 days, often with pruritus and desquamation of overlying skin.



A 30-year-old man has erythrodermic psoriasis and arthritis mutilans involving several digits in both hands.

What would be the most logical treatment for him, leaving out consideration of current NICE guidance?

A Phototherapy

B Prednisolone

C Sulfasalazine

D Methotrexate

E Etanercept

A	Phototherapy
B	Prednisolone
C	Sulfasalazine
D	Methotrexate
E	<b>Etanercept</b>

## Explanation

### Treatment of psoriasis with joint disease

Anti-tumour necrosis factor alpha (TNF- $\alpha$ ) agents (eg etanercept) have been found to be highly effective in the treatment of severe skin and joint disease due to psoriasis. Whilst currently not licenced as first-line choice in the UK, etanercept probably does represent the most effective choice here.

Oral corticosteroids can destabilise the skin disease and are best avoided. Phototherapy should not be given in people with erythrodermic psoriasis. Sulfasalazine is useful in milder polyarticular forms of the disease. Methotrexate is a good alternative but can cause bone marrow suppression and liver damage.

A 24-year-old man presents with myalgia, arthralgia, fever and abdominal pain. On examination, his pulse is 110/minute and his blood pressure is 180/100 mmHg. His abdomen is tender, with guarding, and bowel sounds are absent.

What is the probable diagnosis?

- A Polyarteritis nodosa
- B Behçet's disease
- C Takayasu's arteritis
- D Wegener's granulomatosis
- E Polymyalgia rheumatica

A	Polyarteritis nodosa
B	Behçet's disease
C	Takayasu's arteritis
D	Wegener's granulomatosis
E	Polymyalgia rheumatica



# Explanation

## Differential diagnosis of polyarteritis nodosa

Classic polyarteritis nodosa is a necrotising vasculitis. All age groups can be affected. Hepatitis B is a risk factor. The characteristic presentation is with myalgia, arthralgia, fever and weight loss. Mesenteric vasculitis can cause bowel ischaemia and infarction.

Behçet's disease is a vasculitis of unknown aetiology that characteristically targets venules. There is a strong association with HLA B51. Oral ulcers are common. Unlike aphthous ulcers, they are usually deep and multiple and last for 10–30 days. Genital ulcers are less common (60–80%). Skin lesions include erythema nodosum, pseudofolliculitis, papulopustular lesions or acneiform nodules.

Takayasu's arteritis is a chronic inflammatory granulomatous panarteritis of the major arteries – the carotid, innominate and subclavian arteries and the ascending arch of the aorta. The brachial, radial and ulnar arteries can also be involved. The usual presentation is with claudication and systemic symptoms of fever, arthralgia and weight loss.

Wegener's granulomatosis commonly presents with upper airway involvement (typically epistaxis, nasal crusting and sinusitis), haemoptysis, mucosal ulceration and deafness due to serous otitis media.

Polymyalgia rheumatica is a clinical syndrome of muscle pain and stiffness and an increased erythrocyte sedimentation rate (ESR). It is predominantly a disease of the elderly.

A 20-year-old woman complains of a 2-week history of fever, chest pain, stiffness, swelling in the wrists and fingers and oedema in both legs. She also has a rash on her palms and complains of excessive loss of hair while combing.

Given the likely diagnosis, which one of the following investigation results is most likely to be found on blood testing?

- |   |                                     |
|---|-------------------------------------|
| A | Autoimmune haemolytic anaemia       |
| B | Positive rheumatoid factor          |
| C | Low serum complement levels         |
| D | Anti double-stranded DNA antibodies |
| E | Anticardiolipin antibodies          |

- |   |                                     |
|---|-------------------------------------|
| A | Autoimmune haemolytic anaemia       |
| B | Positive rheumatoid factor          |
| C | Low serum complement levels         |
| D | Anti double-stranded DNA antibodies |
| E | Anticardiolipin antibodies          |

## Explanation

### Serology in SLE

This patient most probably has systemic lupus erythematosus (SLE), given the clinical features. SLE is nine times more common in women and the age of onset is usually between 15 and 25 years.

Owing to the formation of immune complexes, serum complement levels are invariably reduced during active disease. Hence this is the test most likely to be positive in this case. Rheumatoid factor is positive in 25% and anticardiolipin antibodies are present in 35–45% of cases. anti-dsDNA occurs in around half the patients, but may be positive in around 80% of patients with severe systemic involvement. Autoimmune haemolytic anaemia may occasionally occur in this condition.



A 70-year-old woman has a 20-year history of rheumatoid arthritis. One year ago her gold therapy was discontinued because it was found to be ineffective in controlling her arthritis. She was started and then maintained on d-penicillamine (375 mg). Two weeks ago she noticed increased difficulty in climbing stairs. Her husband, who accompanied her, added that he had to wash her hair in the last 4 days.

On examination, she has synovial swelling at the metacarpophalangeal and proximal interphalangeal joints of both hands as well as both knees. Neck and shoulder movements are very restricted. Neurological assessment reveals: grade 3/5 weakness in both upper and lower muscle groups. There is patchy loss of fine touch and pinprick sensation impaired to the abdomen without a clear sensory level being obtained. Deep tendon reflexes are brisk throughout, including upper limbs. The Babinski sign is extensor bilaterally.

The most probable cause of her recent weakness is which of the following?

A	Spinal cord compression due to cervical myelopathy from atlanto-axial subluxation
B	D-penicillamine induced myasthenia gravis
C	Peripheral neuropathy associated rheumatoid arthritis
D	Parasagittal cerebral rheumatoid nodule
E	Generalised weakness due to disuse muscle atrophy secondary to chronic arthritis



A	Spinal cord compression due to cervical myelopathy from atlanto-axial subluxation
B	D-penicillamine induced myasthenia gravis
C	Peripheral neuropathy associated rheumatoid arthritis
D	Parasagittal cerebral rheumatoid nodule
E	Generalised weakness due to disuse muscle atrophy secondary to chronic arthritis

# Explanation

## Atlanto-axial subluxation

### Presenting features

This patient exhibits features of upper motor neurone signs affecting the upper and lower limbs. The most probable diagnosis is cervical myelopathy secondary to her rheumatoid arthritis. The hallmark symptom of cervical myelopathy is weakness or stiffness in the legs and weakness or clumsiness of the hands. Loss of sphincter control or frank incontinence is rare, but some patients may complain of slight hesitancy on urination.

### Examination findings and investigation

A characteristic physical finding of cervical myelopathy is hyperreflexia. Ankle clonus and Babinski's sign (pathological extension of the great toe elicited by stroking the foot) in the feet may also be revealed. Magnetic resonance imaging of the cervical spine is the procedure of choice during the initial screening process of patients with suspected cervical myelopathy.

### Differential diagnosis

In myasthenia gravis and disuse muscle atrophy Babinski's sign is negative. Subcutaneous rheumatoid nodules occur in 20-25% of patients. It is usually observed at areas subject to pressure, such as the elbows, occiput or sacrum (the central nervous system is usually spared).

A 60-year-old man presents with a cough and intermittent haemoptysis, which he has had for 3 months. He has a smoking history of 50 pack-years and is waiting for a bronchoscopy because his chest X-ray showed a left lower lobe collapse. He also complains of muscle weakness and wasting of the proximal muscles of the shoulder and pelvic girdles. His wife says he has been unable to eat solids lately.

Which one of the following statements is true?

- A His dysphagia is due to compression by the tumour
- B He almost certainly has adenocarcinoma of the lung
- C Examination of his fingers will show only clubbing
- D He may have a photosensitive facial rash
- E Corticosteroids have no role in his treatment

- |          |  |
|----------|--|
| A        | His dysphagia is due to compression by the tumour  |
| B        | He almost certainly has adenocarcinoma of the lung |
| C        | Examination of his fingers will show only clubbing |
| <b>D</b> | <b>He may have a photosensitive facial rash</b>    |
| E        | Corticosteroids have no role in his treatment      |

## Explanation

### Dermatomyositis

This patient has a left lower lobe collapse and, with a history of smoking and haemoptysis and cough, the diagnosis is most likely carcinoma of the lung. The association of weakness and wasting of the proximal muscles of the shoulder and pelvic girdles makes dermatomyositis a strong possibility. This is characterised by a photosensitive facial skin and inflammation of the eyelids. Fingers usually show ragged cuticles and haemorrhages, with nail-fold capillary dilatation. Corticosteroids help the muscle weakness and may also clear the cutaneous changes.



A 14-year-old boy attends the clinic with a 1-day history of pain and swelling in his left knee. He is known to have factor VIII deficiency. On examination there is restriction of joint movement. The joint is hot, swollen and extremely painful. The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels are normal. Test for rheumatoid factor is negative.

What is the most likely diagnosis?

A	Pyogenic arthritis
B	Juvenile rheumatoid arthritis
C	Haemophilic arthritis
D	Juvenile chronic arthritis
E	Rickets

A	Pyogenic arthritis
B	Juvenile rheumatoid arthritis
C	Haemophilic arthritis
D	Juvenile chronic arthritis
E	Rickets

## Explanation

### Juvenile arthritis

- + This boy has haemophilic arthritis. The pain and swelling is due to bleeding within the joint.
- + The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels would be raised in pyogenic arthritis.
- + 'Juvenile chronic arthritis' is the term given to a spectrum of arthritides occurring in childhood. Other subgroups are juvenile rheumatoid arthritis (rheumatoid factor is positive), juvenile ankylosing spondylitis, psoriatic arthritis and enteropathic arthritis.
- + In rickets there is a normal amount of bony tissue but reduced mineral content due to vitamin D and calcium deficiency. Knock-knees/bow-legs and hypocalcaemia are features of this condition.

A 42-year-old alcoholic man is admitted with pain, swelling and redness over the first metacarpophalangeal joint. On examination he has a number of tophi, and this is diagnosed as gout. He is started on allopurinol and discharged. Two days later he returns complaining of pain and inflammation over the small joints of his hands, wrists, ankles and knees.

On examination, his temperature is 38.5 °C. Blood tests show: haemoglobin 11.0 g/dl, white cell count  $6.9 \times 10^9/l$ , platelets  $145 \times 10^9/l$ , sodium 138 mmol/l, potassium 4.0 mmol/l, creatinine 90  $\mu\text{mol/l}$ .

Which one of the following is the most likely cause of his presentation?

- A Allergy to allopurinol
- B Septic arthritis
- C Rheumatoid arthritis
- D Pseudogout
- E Allopurinol therapy

## Explanation

### Allopurinol treatment of gout

Treatment of patients presenting with an acute exacerbation of gout using allopurinol alone may precipitate a severe acute attack, including pyrexia. For this reason it is more usual to begin allopurinol in conjunction with an appropriate non-steroidal anti-inflammatory drug (NSAID) or to begin the NSAID a few days before the allopurinol. Given that this patient was an alcoholic, however, the risks of using a NSAID might have been deemed too great in this case. One possible alternative is colchicine, but patients can find this difficult to tolerate on occasions owing to diarrhoea.



A young man who works as a clown in a circus attends the Rheumatology Clinic with a history of recurrent dislocation of his right shoulder. He also complains of increasing pain and stiffness in his left hip. On examination, his height is 150 cm and there is evidence of skin laxity and bruising.

What is the most likely diagnosis?

- |   |                            |
|---|----------------------------|
| A | Marfan's syndrome          |
| B | Ehlers-Danlos syndrome     |
| C | McCune-Albright's syndrome |
| D | Acromegaly                 |
| E | Homocystinuria             |

# Explanation

## Ehlers-Danlos syndrome

Ehlers-Danlos syndrome is characterised by generalised hypermobility, skin laxity and easy bruising, with scoliosis, short stature and ocular fragility. It is a congenital disorder of collagen synthesis in which the capillaries are poorly supported by subcutaneous collagen and ecchymoses are frequently seen

You are called to see an 8-year-old boy who has had a fever of unknown origin for the last 7 days. He also complains of redness of both eyes, redness and dryness of his lips and neck swelling. A rash on his trunk disappeared 2 days ago. On examination he has cervical lymphadenopathy and his palms and soles are red and oedematous.

What is the most likely diagnosis?

- |   |                                    |
|---|------------------------------------|
| A | Infectious mononucleosis           |
| B | AIDS                               |
| C | Kawasaki disease                   |
| D | Acute systemic lupus erythematosus |
| E | Sjögren's syndrome                 |

# Explanation

## Kawasaki disease

Kawasaki disease is a clear-cut clinical entity that can be diagnosed after the recognition and analysis of six main symptoms:

- + Fever of unknown aetiology lasting 5 days or more. In general, the onset of Kawasaki disease is with abrupt high fever but without prodromal symptoms such as coughing, sneezing or rhinorrhoea. Usually the fever is either remitting or continuous, ranging from 38 °C to 40 °C for 1-2 weeks.
- + Bilateral congestion of ocular conjunctiva. Conjunctival infection develops 2-4 days after the onset of fever.
- + Changes to the lips and oral cavity. Dryness, redness and fissuring of the lips occur 3-5 days after the onset of fever. The membranes of the oral cavity and pharyngeal mucosa are diffusely red. There is no vesicle, aphtha or pseudomembrane formation.
- + Acute non-purulent swelling of cervical lymph nodes - from the day before the onset of fever, or together with the fever, there is swelling of the cervical lymph nodes.
- + Polymorphous exanthema. From day 1-5 after the onset of fever, a polymorphic rash appears on the trunk or extremities. It is variously morbilliform, scarlatiniform, urticariform or erythema multiforme-like. In each case the rash is a different combination of these forms. They are not accompanied by vesicles or crusts, but sometimes there are small aseptic pustules on the knees, buttocks or other sites. The eruptions usually disappear in less than a week.
- + Changes to the extremities. Approximately 2-5 days after the onset of the disease, when the rash on the trunk has appeared, there is reddening of the palms and soles.



A 70-year-old man has been experiencing a right-sided headache and severe temporomandibular joint pain for the past week. He now presents with a sudden loss of vision in his right eye.

What treatment is required urgently to avoid vision loss in the left eye?

A Intraocular steroids

B Intravenous steroids

C Pilocarpine

D Timolol

E Sumatriptan

A Intraocular steroids

**B Intravenous steroids**

C Pilocarpine

D Timolol

E Sumatriptan

## Explanation

### Temporal arteritis

This man has giant-cell arteritis affecting the temporal artery. This is an inflammatory granulomatous arteritis of large arteries, which occurs in association with polymyalgia rheumatica. Involvement of the ophthalmic arteries causes a sudden painless temporary or permanent visual loss. Corticosteroids are obligatory in this condition because they significantly reduce the risk of irreversible visual loss and other focal ischaemic lesions. Intravenous steroids are indicated when there is sudden unilateral loss of vision to avoid vision loss in the other eye.

A 67-year-old man with poorly controlled seropositive rheumatoid arthritis for 22 years is followed up in Outpatients. He has noticed swelling around the eyes, especially first thing in the morning. Routine urinalysis reveals that he has +++ protein. His current medication includes methotrexate 20 mg weekly, sulfasalazine 1 g twice daily, prednisolone 5 mg once a day and ibuprofen 400 mg three times a day.

What is the likely diagnosis?

- A IgA nephropathy
- B Amyloidosis
- C Rheumatoid vasculitis
- D Drug-induced nephropathy
- E Renal tubular acidosis

## Explanation

### Amyloidosis

Periorbital oedema and +++ of proteinuria is suggestive of the nephrotic syndrome. In rheumatoid arthritis drugs that cause this are gold and penicillamine (neither of which he is on). The clue is in the long duration of uncontrolled disease, suggesting the rare complication of amyloid A (AA) amyloidosis.

Of the other options, rheumatoid vasculitis is very rare and is almost never associated with renal disease. A non-steroidal anti-inflammatory drug (NSAID) nephropathy does not normally result in nephrotic syndrome. Adequate control of his rheumatoid arthritis may slow any worsening of his amyloidosis.



A middle-aged woman with a history of rheumatoid arthritis presents with right foot drop and numbness in her right hand, with thenar eminence wasting and sensory loss over the radial half of her hand.

What is the most likely cause of her symptoms?

A Peripheral sensory neuropathy

B Mononeuritis multiplex

C Entrapment neuropathy

D Myasthenia gravis

E Multiple sclerosis

# Explanation

## Mononeuritis multiplex

The presence of multifocal concurrent peripheral nerve lesions and the absence of symptoms such as pain and paraesthesiae in this case suggest mononeuritis multiplex as the most likely cause for her symptoms. This patient has a right median nerve and a right peroneal nerve lesion.

Mononeuritis multiplex is a neuropathy of two or more peripheral nerves that are not anatomically related. Pathologically, the nerves are made susceptible to mechanical compression by ischaemia caused by vasculopathy of the vasa nervorum or infiltration of the nerves.

Common causes are:

- + Diabetes mellitus
- + Leprosy
- + Polyarteritis nodosa
- + Rheumatoid arthritis

## Differential diagnosis

- + Multiple sclerosis affects the central nervous system (spinal cord and brainstem lesions are common). This can cause spasticity, ataxia and dysaesthesia in the affected limbs. Optic neuritis is an early and characteristic manifestation of this condition. Peripheral nerve involvement is not seen.
- + In myasthenia gravis distal limb involvement is uncommon early in the disease: the extraocular, bulbar, face and neck muscles are commonly affected first.
- + Motor weakness and muscle wasting do not accompany peripheral sensory neuropathy.
- + Entrapment neuropathies result from compression of peripheral nerves due to hypertrophied synovium or joint subluxation. Median nerve compression in the carpal tunnel is the most common, and bilateral compression can be an early clinical manifestation of rheumatoid arthritis. Aching pain and paraesthesia characteristically occur in the distal affected parts, followed by sensory loss and muscle wasting.

A 25-year-old salesman complains he has had morning back pain and stiffness for the last 5 months. He also complains of intermittent red and itchy eyes and arthralgia of his knees and elbows. He has a raised erythrocyte sedimentation rate (ESR) but the other blood test results are normal. A radiograph of the lumbar spine has been taken.

What is the most likely radiographic finding?

A	Bony metastasis
B	Wedge fractures of the vertebrae
C	Rugger-jersey spine
D	Extensive osteophyte formation
E	Tramline appearance



- |   |                                  |
|---|----------------------------------|
| A | Bony metastasis                  |
| B | Wedge fractures of the vertebrae |
| C | Rugger-jersey spine              |
| D | Extensive osteophyte formation   |
| E | <b>Tramline appearance</b>       |

## Explanation

### Radiographic appearances in ankylosing spondylitis

This man has ankylosing spondylitis. The tramline appearance is due to syndesmophyte growth between the margins of the vertebrae as well as calcification and ossification of the interspinous ligaments. X-ray of the pelvis will show fusion of the sacroiliac joints.

A 22-year-old coal miner presents at the Emergency Department with exertional dyspnoea and wheezing, right foot drop, weakness in his left hand, a purpuric rash over his abdomen and swollen ankles. Blood tests show: haemoglobin 12.3 g/dl, mean corpuscular volume (MCV) 92 fl, white cell count (WCC)  $21.4 \times 10^9/l$  (neutrophils  $8.0 \times 10^9/l$ , eosinophils  $10.2 \times 10^9/l$ , lymphocytes  $2.5 \times 10^9/l$ ); urea 18.9 mmol/l, creatinine 270  $\mu\text{mol/l}$ ; cytoplasmic antineutrophil cytoplasmic antibody (cANCA) negative, perinuclear antineutrophil cytoplasmic antibody (pANCA) positive.

What is the most probable diagnosis?

- |   |                          |
|---|--------------------------|
| A | Wegener's granulomatosis |
| B | Caplan's syndrome        |
| C | Polyarteritis nodosa     |
| D | Churg-Strauss syndrome   |
| E | Microscopic polyangiitis |

# Explanation

## Churg-Strauss syndrome

Churg-Strauss syndrome is a variant of polyarteritis nodosa (PAN). It occurs in patients, usually male, who have a triad of rhinitis and asthma, eosinophilia and systemic vasculitis. Unlike PAN, it is a small-vessel necrotising granulomatous disease that principally affects the lungs, peripheral nerves and skin. The typical acute presentation is with skin lesions (purpura or nodules), asymmetrical mononeuritis multiplex, eosinophilia and asthma. Perinuclear antineutrophil cytoplasmic antibody (pANCA) may be positive in this condition. Kidney involvement is less common but is known to occur.

## Differential diagnosis

Microscopic vasculitis (polyangiitis) involves the kidneys and the lungs where it results in recurrent haemoptysis. In earlier literature there was confusion between this condition, Churg-Strauss syndrome and polyarteritis nodosa. Polyarteritis nodosa, however, is pANCA-negative and rarely involves the lungs. Microscopic vasculitis presents with rapidly progressive glomerulonephritis often associated with alveolar haemorrhage.

A 42-year-old woman with seropositive rheumatoid arthritis has become disabled by pain and tightness behind the right knee. Physical examination reveals a cystic swelling over the popliteal fossa and semimembranosus tendon.

Which one of the following is the most appropriate next step?

- |   |  |
|---|--|
| A | Magnetic resonance imaging (MRI) of the right knee |
| B | Synovial biopsy of the right knee                  |
| C | Ultrasound study of the right knee popliteal fossa |
| D | Venogram of right lower extremity                  |
| E | Arthroscopy of the right knee                      |



- |   |  |
|---|--|
| A | Magnetic resonance imaging (MRI) of the right knee |
| B | Synovial biopsy of the right knee                  |
| C | Ultrasound study of the right knee popliteal fossa |
| D | Venogram of right lower extremity                  |
| E | Arthroscopy of the right knee                      |

## Explanation

### Baker's cyst

The physical examination is suggestive of a distended Baker's cyst, but physical examination alone is not diagnostic, particularly if there has been a dissection or rupture.

Ultrasonography has been found to be very useful in making a diagnosis of popliteal cyst, with or without dissection, and is likely to be more readily available than magnetic resonance imaging. An arthrogram could also demonstrate a popliteal cyst but is less desirable because it is an invasive procedure. A venogram of the right lower extremity could be performed if a deep vein thrombosis was suspected clinically but would not be indicated in this case.

A 50-year-old woman presents with a 4-month history of Raynaud's phenomenon, progressive skin tightness, thickness of the fingers and hands, dyspnoea on exertion and dysphagia.

What is the most probable diagnosis?

- |   |                               |
|---|-------------------------------|
| A | Limited cutaneous scleroderma |
| B | Diffuse cutaneous scleroderma |
| C | Rheumatoid arthritis          |
| D | Sarcoidosis                   |
| E | Systemic lupus erythematosus  |

# Explanation

## Diffuse cutaneous scleroderma

Diffuse cutaneous scleroderma starts with swelling and stiffness of the fingers and is followed by the development of extensive sclerosis. Heartburn, reflux or dysphagia are almost invariable. Raynaud's phenomenon usually starts just before or at the onset of the disease, in contrast to limited cutaneous scleroderma, in which Raynaud's phenomenon precedes the disease by many years. Renal involvement can be acute or chronic and can lead to hypertension. Lung disease, both fibrosis and pulmonary hypertension, contribute significantly to mortality.

Sarcoidosis presents classically as bilateral hilar lymphadenopathy on chest X-ray. It is asymptomatic in a third of cases. Dysphagia is usually not a feature. Raynaud's phenomenon is not a feature of rheumatoid arthritis. Pulmonary symptoms are usually a feature of long-standing rheumatoid arthritis. Systemic lupus erythematosus is a non-organ-specific autoimmune disease characterised by antinuclear antibodies and vasculitis. It usually presents earlier, in the younger woman. Progressive skin tightness and dysphagia are not seen in this condition.

A 62-year-old, previously fit man presents with a 2-month history of fatigue, exertional dyspnoea and abdominal pain. He also has evidence of severe arthritis in his hands and progressive numbness of his feet. On examination, red spots are noted on the extensor surfaces of his lower limbs. An X-ray of the chest shows cardiomegaly.

What diagnosis is best suggested by these findings?

A	Rheumatoid arthritis
B	Sarcoidosis
C	Polymyalgia rheumatica
D	Dermatomyositis
E	Polyarteritis nodosa



# Explanation

## Polyarteritis nodosa

Polyarteritis nodosa (PAN) may present with all these features. PAN is a necrotising vasculitis that causes aneurysms of medium-sized arteries. Abdominal pain due to infarction of a viscus, dyspnoea due to pulmonary infiltrates, arthralgia and purpuric spots can all occur in this condition.

## Differential diagnosis

- + Sarcoidosis presents classically as bilateral hilar lymphadenopathy on chest X-ray. In a third of patients it presents with cough, fever, arthralgia, malaise or erythema nodosum (painful erythematous nodular lesions on the anterior aspect of the shins). Ventricular tachycardia, complete heart block, cardiomyopathy and pericardial effusion are seen, but cardiomegaly is not a feature.
- + Polymyalgia rheumatica (PMR) occurs commonly in older women and presents as aching and morning stiffness in the proximal muscles.
- + Symmetrical proximal muscle weakness resulting from muscle inflammation is seen in polymyositis. Some 25% of patients have a purple (heliotrope) rash on the cheeks, eyelids and light-exposed areas (dermatomyositis). Cardiac involvement is not seen in PMR or in dermatomyositis.

Fatigue, exertional dyspnoea, abdominal pain and red spots on the shins are not characteristic of rheumatoid arthritis.

A 50-year-old diabetic woman with a history of osteoarthritis of her knees suddenly develops pain and swelling in her right knee. On examination the knee is red, hot, swollen and very tender.

Which investigation would be most helpful in the management of this case?

- |   |  |
|---|--|
| A | Plain X-ray of the knee  |
| B | Joint aspiration, gram stain and culture then start antibiotics                |
| C | Joint fluid microscopy   |
| D | Blood culture and start antibiotics  |
| E | Joint aspiration and culture, start antibiotics when 48 hour culture available |

- |   |  |
|---|--|
| A | Plain X-ray of the knee  |
| B | Joint aspiration, gram stain and culture then start antibiotics                |
| C | Joint fluid microscopy   |
| D | Blood culture and start antibiotics  |
| E | Joint aspiration and culture, start antibiotics when 48 hour culture available |

## Explanation

### Septic arthritis

Aspiration of the joint and urgent Gram-staining will confirm the diagnosis of septic arthritis. X-rays normally show no change in septic arthritis, as the onset is acute. Joint fluid microscopy is useful in acute gouty arthritis. This would show the characteristic long needle-shaped uric acid crystals in the fluid as well as in neutrophils. A joint already damaged due to osteoarthritis is more likely to become septic. The features in this case are more in favour of septic arthritis than acute gouty arthritis. Treatment cannot await the results of blood culture and joint aspirate culture, but should be started immediately on finding organisms in the aspirate (ie but before an organism is actually identified).

A 20-year-old football player presents with a swollen left knee and locking. He complains of pain after exercise. On examination, wasting over the quadriceps and lateral aspect of the joint are noted. Arthroscopy of the joint reveals three loose bodies in the synovial cavity.

What is the most likely diagnosis?

A Chip fractures of the joint surfaces

B Osteoarthritis

C Synovial chondromatosis

D Osteochondritis dissecans

E Semi-lunar cartilage tear



## Explanation

### Osteochondritis dissecans

Osteochondritis dissecans is local necrosis of the articular cartilage and its underlying bone, which results in a loose body leaving the surrounding bone. The cause is unknown. The medial femoral condyle is most commonly affected and the condition is seen in adolescents and young adults. Either three or four loose bodies might be present in the knee.

### Differential diagnosis

- + Usually one or two loose bodies may be seen in chip fractures of joint surfaces.
- + Multiple loose bodies (> 50) are seen in synovial chondromatosis, but this condition is rarely associated with pain.
- + Semilunar cartilage tears occur as a result of a forcible twist to the flexed knee (eg while playing football). Extension is limited as the displaced segment lodges between the femoral and tibial condyles. Loose bodies are not seen in this condition.

Osteoarthritis is unlikely at this age. In osteoarthritis there can be as many as 10 loose bodies.

A 55-year-old man attends the clinic complaining of increasing pain and weakness of his lower limbs which is preventing him from getting up from a chair easily and from climbing the stairs. Blood tests show a creatinine kinase level of 14,500 IU/l. A chest X-ray reveals a large shadow in the right mid-zone and pulmonary function tests reveal evidence of pulmonary fibrosis.

Which antibody is most strongly associated with this disease?

A Anti-centromere

B Anti-Jo-1

C Anti-RNP

D Anti-Scl-70

E Anti-dsDNA

A	Anti-centromere
B	Anti-Jo-1
C	Anti-RNP
D	Anti-Scl-70
E	Anti-dsDNA

## Explanation

### Polymyositis

This patient has polymyositis, which is often associated with an increased risk of malignancy (threefold). The typical presentation is with symmetrical proximal muscle weakness, usually affecting the lower extremities first. Creatine kinase is usually elevated and is a guide to disease activity. Antisynthetase (Anti-Jo-1) antibodies are strongly associated with polymyositis.

A 75-year-old woman presents with early morning stiffness and pain in both shoulders and hips. On examination, active movements in these joints are restricted due to pain, but passive movements are preserved. She has no other symptoms. Blood tests are normal, except for an erythrocyte sedimentation rate (ESR) of 115 mm in 1st hour and a C-reactive protein (CRP) of 4.9 mg/l. Her bone densitometry T-score value is -1.5.

What are her symptoms due to?

- |   |                             |
|---|-----------------------------|
| A | Osteoarthritis              |
| B | Rheumatoid arthritis        |
| C | Polymyositis                |
| D | Polymyalgia rheumatica      |
| E | Postmenopausal osteoporosis |



# Explanation

## Polymyalgia rheumatica

Polymyalgia rheumatica is associated with muscle pain and stiffness and an increased erythrocyte sedimentation rate (ESR). It is not a true vasculitis but is closely associated with giant-cell arteritis. Women are more commonly affected than men (the ratio of women to men affected is 2:1). The muscle stiffness affects the proximal muscles of the neck, upper arms and, less commonly, the buttocks and thighs. There is marked early morning stiffness. The C-reactive protein (CRP) may be elevated prior to the ESR.

## Differential diagnosis

Polymyositis is common at a younger age (40–60 years) and is typically gradual. Systemic features of fever, weight loss and fatigue are common. There may be respiratory or pharyngeal muscle involvement leading to ventilatory failure or aspiration. The creatine kinase is usually elevated in this condition.

A bone mass density T-score of -1.5 indicates that there is no osteoporosis at present, but there is a risk of developing osteoporotic complications unless preventive measures are undertaken. The clinical picture is not suggestive of either osteoarthritis or rheumatoid arthritis.

A 40-year-old woman with sickle cell disease complains of severe right hip pain for the past week; she has had milder pain in the same hip for up to 3 months. She walks with a limp and has a positive Trendelenburg's sign. There is a tendency for the hip to twist into internal rotation during passive flexion. Blood culture is negative. An X-ray of the hip appears normal.

What is the most likely diagnosis in this case?

- |   |   |
|---|---|
| A | Septic arthritis                        |
| B | Avascular necrosis of the femoral head  |
| C | Osteomyelitis of the femur              |
| D | Pathological fracture of the femur neck |
| E | Osteoarthritis of the hip               |

## Explanation

### Avascular necrosis of the femoral head

This patient most probably has avascular necrosis of the femoral head. The femoral head is the commonest site of avascular necrosis because its peculiar blood supply that makes it vulnerable to ischaemia. Ischaemia is common in sickle cell disease.

### Differential diagnosis

- + Septic arthritis would be associated with a swollen inflamed hip joint and systemic features such as fever. Movement on the joint would not be possible. X-ray findings would not be conclusive.
- + Osteomyelitis is more common in the distal femur. The joint is usually kept immobile and there would be warmth and tenderness over the affected part. There may be signs of systemic infection. Although X-ray changes are not apparent early in the disease, after a few days there would be haziness and loss of density of the affected bone, followed by subperiosteal reaction.
- + A pathological fracture of the femoral head usually occurs after a fall, rarely spontaneously unless there is severe osteoporosis. Weight bearing is painful or impossible and the leg is usually shortened and externally rotated. The fracture might be evident on X-ray.
- + Osteoarthritis of the hip is uncommon in women at this age, unless the hip has been damaged due to rheumatoid arthritis or ankylosing spondylitis.



A 34-year-old man presents with severe unremitting pain affecting the left leg. Three months earlier he had an arthroscopic wash-out for septic arthritis affecting his left knee caused by a penetrating injury. Examination reveals a markedly reduced range of movement of the left knee with diffuse swelling of the left leg and overlying cool dry scaly skin.

What is the likely diagnosis?

- |   |                                   |
|---|-----------------------------------|
| A | Ongoing septic arthritis          |
| B | Underlying deep venous thrombosis |
| C | Reactive arthritis                |
| D | Reflex sympathetic dystrophy      |
| E | Reiter's syndrome                 |



## Explanation

### Reflex sympathetic dystrophy

The description here is compatible with a diagnosis of reflex sympathetic dystrophy (complex regional pain syndrome) that has developed following the previous injury. The pain is often severe and disproportionate to the signs and follows a non-anatomical distribution. The skin changes are caused by the associated autonomic dysfunction.

A 62-year-old woman complains of general lethargy, morning stiffness and inability to comb her hair because of arm pain. There is no muscle tenderness although she says there is pain on movement of the shoulders and hips. Her erythrocyte sedimentation rate (ESR) is 57 mm in 1st hour. Electromyography of the deltoid muscle is normal.

What is the most likely diagnosis?

A	Guillain-Barré syndrome
B	Polymyositis
C	Polymyalgia rheumatica
D	Multiple sclerosis
E	Fibromyalgia

# Explanation

## Polymyalgia rheumatica

Polymyalgia rheumatica (PMR) occurs more commonly in the elderly, particularly women, and presents as aching and morning stiffness in the proximal muscles. PMR is a form of giant-cell arteritis. The diagnosis is made on the basis of the history and symptoms. The erythrocyte sedimentation rate (ESR) is almost always remarkably high ( $> 40$  mm in 1st hour).

### Differential diagnosis

- + Guillain-Barré syndrome (acute postinfective polyneuritis) presents with back and limb pain, followed by progressive ascending paralysis.
- + Symmetrical proximal muscle weakness resulting from muscle inflammation is seen in polymyositis. Electromyography would show the typical triad of changes with myositis: spontaneous fibrillation potentials at rest, polyphasic or short-duration potentials on voluntary contraction, and salvos of repetitive potentials on mechanical stimulation of the nerve.
- + Multiple sclerosis presents mostly with unilateral optic neuritis or progressive weakness of the legs. The most common age of onset of this disease is between 20 and 45 years.
- + Fibromyalgia classically presents with diffuse pain and multiple tender spots all over the body that might be anatomically unrelated to the affected muscles. The erythrocyte sedimentation rate (ESR) is normal in this condition.

A 42-year-old woman complains of nocturnal tingling and pain in her right hand. The pain is reproduced on tapping over the median nerve at the wrist.

Given the probable explanation for her symptoms, what is the likeliest underlying cause?

A Rheumatoid arthritis

B Hypothyroidism

C Idiopathic

D Acromegaly

E Pregnancy



A Rheumatoid arthritis

B Hypothyroidism

C Idiopathic

D Acromegaly

E Pregnancy

## Explanation

### Carpal tunnel syndrome

This patient most probably has carpal tunnel syndrome, which is a common condition causing median nerve compression at the wrist. All of the conditions listed above may cause carpal tunnel syndrome, however, the majority of cases are idiopathic. There is nocturnal tingling and pain in the hand (and forearm at times), followed by weakness of the thenar muscles.

A 35-year-old daughter has just been diagnosed with rheumatoid arthritis. She attends the clinic with her mother, who has a severe form of the disease. She is considering having children but is worried that they too might inherit the condition. They have a number of questions about heritability, including about HLA associations with rheumatoid arthritis.

Which one of the following HLA antigens is known to be associated with the development of rheumatoid arthritis?

- |   |         |
|---|---------|
| A | HLA B5  |
| B | HLA B27 |
| C | HLA DR4 |
| D | HLA B7  |
| E | HLA B8  |

A	HLA B5
B	HLA B27
C	HLA DR4
D	HLA B7
E	HLA B8

## Explanation

### HLA antigens

Human leucocyte-associated (HLA) antigens DR1 and DR4 are associated with rheumatoid arthritis and primary sclerosing cholangitis, whereas HLA B27 is associated with increased risk of seronegative arthritides and inflammatory bowel disease. HLA B8 and HLA DR3 are associated with an increased risk of Graves' disease and HLA B7 is thought to be protective. HLA B5 are thought to be associated with an increased risk of Behçet's disease. Different HLA antigen patterns are thought to confer differing risks to tissue-specific autoimmune diseases.

A 14-year-old girl, who is otherwise fit, complains of backache and fatigue. Her parents have also noticed that she is increasingly becoming round-shouldered. On examination, movements are normal. A smooth lump is seen in the thoracic region.

What would be the most characteristic feature of an X-ray of the thoracic spine?

A	Anterior displacement of one thoracic vertebra upon another
B	Absent neural arch
C	Osteophyte formation on posterior facet joints
D	Irregular upper and lower vertebral endplates with loss of disc space height
E	Scoliosis



- |   |  |
|---|--|
| A | Anterior displacement of one thoracic vertebra upon another                  |
| B | Absent neural arch   |
| C | Osteophyte formation on posterior facet joints                               |
| D | Irregular upper and lower vertebral endplates with loss of disc space height |
| E | Scoliosis  |

## Explanation

### Scheuermann's disease

This girl has Scheuermann's disease. It usually affects those between 13 and 16 years of age. The normal ossification of ring epiphyses of several thoracic vertebrae is affected. Deforming forces are greatest at the anterior border of the vertebrae so vertebrae are narrower anteriorly, resulting in kyphosis. Kyphosis, and not scoliosis, is the presenting feature of Scheuermann's disease.

Anterior displacement occurs in spondylolisthesis (a defect in the pars interarticularis of the neural arch). Osteophyte formation is seen in osteoarthritis.

A 62-year-old woman is admitted to the psychiatric ward with delusions that her neighbours are trying to poison her. She is later discharged on chlorpromazine, her behaviour having returned to normal. However, she then presents a few weeks later with joint pains and a dry mouth. Investigations show: haemoglobin 12.4 g/dl, white cell count  $6.1 \times 10^9/l$ , platelets  $167 \times 10^9/l$ , sodium 139 mmol/l, potassium 4.5 mmol/l, creatinine 134  $\mu\text{mol/l}$ , alanine aminotransferase (ALT) 36 U/l, anti-single-stranded DNA positive, anti-Ro positive, C4 slightly reduced.

Which one of the following is the most likely diagnosis?

- |   |                                  |
|---|----------------------------------|
| A | Drug induced lupus               |
| B | SLE                              |
| C | Sjogren's                        |
| D | Mixed connective tissue disorder |
| E | Scleroderma                      |

# Explanation

## Drug-induced lupus

The proximity of this lady's onset of symptoms to the commencement of chlorpromazine is inescapable. Often the only symptoms of drug-induced lupus are joint pains and these have clearly been reported here. Anti-single-stranded DNA positivity is more commonly seen in drug-induced lupus than in systemic lupus erythematosus (SLE) and anti-Ro positive antibodies are seen, particularly in conjunction with hydrochlorothiazide use. Complement levels tend to be either normal or only slightly reduced, compared with the more marked reductions seen in active SLE. Key to confirming the diagnosis of drug-induced lupus is withdrawal of the offending agent coupled with an attendant improvement in symptoms.

## Causes

A number of classes of agents have been implicated in the development of drug-induced lupus, including:

- + Anticonvulsants – carbamazepine, valproate, and ethosuximide
- + Antibiotics – isoniazid
- + Anti-inflammatory drugs – penicillamine, sulfasalazine

A 37-year-old gym instructor gives a 2-year history of numbness and burning of his fingers precipitated by cold. He now feels tightness in his fingers and is unable to extend them completely. He also complains of a progressive difficulty in swallowing food. You suspect limited cutaneous scleroderma.

Which one of the following blood investigations would most aid in the diagnosis?

A	Normocytic normochromic anaemia
B	Microangiopathic haemolytic anaemia
C	Anticentromere antibodies
D	Antinuclear antibodies
E	Rheumatoid factor



- |   |                                     |
|---|-------------------------------------|
| A | Normocytic normochromic anaemia     |
| B | Microangiopathic haemolytic anaemia |
| C | <b>Anticentromere antibodies</b>    |
| D | Antinuclear antibodies              |
| E | Rheumatoid factor                   |

## Explanation

### Limited cutaneous scleroderma

Limited cutaneous scleroderma usually starts with Raynaud's phenomenon many years before the appearance of any skin changes. The skin involvement is limited to the hands, face, feet and forearms. The skin is tight over the fingers and often produces flexion deformities of the fingers. The 'CREST syndrome' was the term previously used to describe this condition - calcinosis of subcutaneous tissues, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly and telangiectasia. Anticentromere antibodies occur in 70-80% of cases, but most are specific to CREST syndrome.

Anaemia, whether normocytic normochromic or haemolytic, is not specific for this condition. Rheumatoid factor is positive in 30% of cases, as are antinuclear antibodies. However, their presence would not aid in the diagnosis.

An 82-year-old woman was hospitalised for treatment of congestive heart failure. She experienced a warm, painful right knee on day 3 of this hospital stay.

Which one of the following would be the most appropriate procedure?

- |   |   |
|---|---|
| A | Blood cultures followed by antibiotics iv                 |
| B | Arthrocentesis for diagnostic/therapeutic purposes        |
| C | Colchicine iv   |
| D | Allopurinol   |
| E | Ultrasound study of right knee, including popliteal fossa |

## Explanation

### Monoarthritis in a patient hospitalised with CCF

Clinically, the patient has a monoarthritis most likely to be crystal-induced (pseudogout or gout). This is particularly likely considering that she will have been aggressively treated with diuretics for her heart failure. She could also have septic arthritis, although this would be less likely, but seeding of infection from other sites in the body is possible, particularly in elderly patients. Gout and pseudogout can be rapidly and definitively diagnosed by proper examination of joint fluid and infection can also be ruled out this way, making arthrocentesis the investigation of choice.

A 22-year-old man who suffers from inflammatory bowel disease has developed pain and stiffness in his lower back over the past 6 months. Examination reveals tenderness over both sacroiliac joints. He tests positive for HLA-B27.

What is the most probable diagnosis?

- |   |                               |
|---|-------------------------------|
| A | Prolapsed intervertebral disc |
| B | Rheumatoid arthritis          |
| C | Ankylosing spondylitis        |
| D | Osteoarthritis                |
| E | Enteropathic arthritis        |



# Explanation

## Ankylosing spondylitis

Ankylosing spondylitis most commonly involves the sacroiliac joints causing pain and stiffness. Up to half the patients have inflammation of the colon or ileum. Although this may be asymptomatic, frank inflammatory bowel disease may develop in 5-10% of cases. The *HLA-B27* gene is present in nearly 90% of patients with ankylosing spondylitis. It is the distribution, with particularly the sacroiliac joints being affected and the absence of a peripheral small joint arthropathy, which fits better with ankylosing spondylitis rather than enteropathic arthritis.

## Differential diagnosis

- + Prolapse of an intervertebral disc is usually associated with severe lower back pain and sciatica. Stiffness is not a feature.
- + Rheumatoid arthritis seldom involves the sacroiliac joints as the primary site.
- + Enteropathic arthritis encompasses various arthritides that are linked to GI pathology, including reactive arthritis associated with GI infection (salmonella, shigella) and spondyloarthritides associated with inflammatory bowel disease (ulcerative colitis or Crohn's disease). This occurs with equal frequency in men and women. Of particular interest is the strong association between reactive arthritis and HLA-B27. A flare-up of the bowel disease triggers attacks of arthritis.
- + Osteoarthritis is unlikely in this age group and is not associated with bowel disease.

A 32-year-old man with rheumatoid arthritis presents with left-sided chest pain. On examination, he is febrile. The electrocardiogram (ECG) shows widespread saddle-shaped ST elevation.

What is the most probable diagnosis?

- |   |                       |
|---|-----------------------|
| A | Pericarditis          |
| B | Cardiac tamponade     |
| C | Myocardial infarction |
| D | Cardiomyopathy        |
| E | Pulmonary fibrosis    |

A	Pericarditis
B	Cardiac tamponade
C	Myocardial infarction
D	Cardiomyopathy
E	Pulmonary fibrosis

## Explanation

### Rheumatoid pericarditis

This patient has acute pericarditis, as suggested by the electrocardiography (ECG) tracing. It is a known extra-articular manifestation of rheumatoid arthritis. Cardiac tamponade is very rare. The ECG does not suggest myocardial infarction or cardiomyopathy. Fibrosing alveolitis is the most common pulmonary manifestation of rheumatoid arthritis. It is not associated with ECG changes.

A 50-year-old woman is concerned about osteoporosis because her mother had it. She had a premature menopause at the age of 40 but no other risk factors in her history. You decide to perform a bone mineral density (BMD) test. This comes back showing a Z-score of 0 and T-score of  $-0.5$  SD.

How do you interpret these results?

- |   |   |
|---|---|
| A | Patient has osteoporosis                                    |
| B | Patient has osteopenia                                      |
| C | Patient has normal BMD for her age                          |
| D | Patient is at risk of fracture and should receive treatment |
| E | Patient has lower than expected BMD for her age             |



- |          |   |
|----------|---|
| A        | Patient has osteoporosis                                    |
| B        | Patient has osteopenia                                      |
| <b>C</b> | <b>Patient has normal BMD for her age</b>                   |
| D        | Patient is at risk of fracture and should receive treatment |
| E        | Patient has lower than expected BMD for her age             |

## Explanation

### Bone mineral density

The T-score represents the bone mineral density (BMD) measurement compared with that which would be obtained from an average person at their peak bone mass. The Z-score is the BMD score compared with a normal individual but adjusted for the age of the person. A Z-score of 0 means that the individual has normal BMD for their age.

The WHO definition of osteoporosis is a T-score of  $-2.5$  standard deviations below the norm or lower. At this level the person is deemed to be at risk of fracture. Osteopenia is defined as a T-score between  $-1$  and  $-2.5$  SD.

A 42-year-old woman presents with swollen, painful finger joints. Rheumatoid factor is positive.

Which one of the following deformities found on clinical examination is most typical of this disease?

- |   |   |
|---|---|
| A | Ulnar deviation of the metacarpophalangeal joints |
| B | Boutonnière deformity                             |
| C | Swan-neck deformity                               |
| D | Spindling of the fingers                          |
| E | Finger drop of the little and ring fingers        |

A	Ulnar deviation of the metacarpophalangeal joints
B	Boutonnière deformity
C	Swan-neck deformity
D	Spindling of the fingers
E	Finger drop of the little and ring fingers

## Explanation

### The hand in rheumatoid arthritis

This patient most probably has rheumatoid arthritis. The most typical deformity in rheumatoid arthritis is a combination of ulnar drift and palmar subluxation of the metacarpophalangeal joints. Fixed flexion (Boutonnière deformity) or fixed hyperextension (swan-neck deformity) of the proximal interphalangeal joints impair hand function. Rupture of the finger extensor tendons may lead to finger drop, predominantly of the little and ring fingers.

A 45-year-old man complains of burning pain in his foot, with diminished sensation in the sole. He twisted his ankle a week earlier. Severe pain and paraesthesiae can be elicited by applying pressure behind the medial malleolus.

What is the most likely cause of his presentation?

- A Atherosclerosis of the popliteal arteries
- B Injury to the tibial nerve
- C Rupture of the Achilles tendon
- D Injury to the common peroneal nerve
- E Compression of the posterior tibial nerve



- |   |   |
|---|---|
| A | Atherosclerosis of the popliteal arteries |
| B | Injury to the tibial nerve                |
| C | Rupture of the Achilles tendon            |
| D | Injury to the common peroneal nerve       |
| E | Compression of the posterior tibial nerve |

## Explanation

### Differential diagnosis of tarsal tunnel syndrome

- + This person has tarsal tunnel syndrome caused by entrapment of the posterior tibial nerve.
- + Burning pain is not a feature of intermittent claudication, where the pain is caused mainly by walking.
- + Rupture of the Achilles tendon causes sudden pain at the back of the ankle during running or jumping. Loss of sensation and burning pain do not occur in this condition.
- + Foot drop is seen with damage to the peroneal nerves. Sensation is lost over the front and outer half of the leg and dorsum of the foot.

A 14-year-old obese boy with left groin pain for the past 6 weeks is noted to be standing with his left leg externally rotated. Examination reveals negligible internal rotation of the hip.

What is the most likely diagnosis?

A Congenital dislocation of the hip

B Juvenile rheumatoid arthritis

C Perthe's disease

D Slipped upper femoral epiphysis

E Osteogenic sarcoma

A Congenital dislocation of the hip

B Juvenile rheumatoid arthritis

C Perthe's disease

**D Slipped upper femoral epiphysis**

E Osteogenic sarcoma

# Explanation

## Groin pain in a teenager

- + Slipped upper femoral epiphysis affects children aged 10–16 years and 20% are bilateral. About half the patients are obese and hypogonadal. Flexion, adduction and medial rotation of the hip are limited.
- + Congenital dislocation of the hip is seen in neonates. Girls are more commonly affected than boys. If not detected in infancy, older children can present with delay in walking, an abnormal waddling gait and an inability to fully abduct the affected hip.
- + Still's disease (juvenile rheumatoid arthritis) occurs mainly in prepubertal girls, with mono- or polyarticular synovitis with erosion of cartilage, often preceded by fevers, iridocyclitis, pneumonitis, lymphadenopathy and splenomegaly. It accounts for 10% of all cases of juvenile chronic arthritis.
- + Perthes' disease is osteochondritis of the femoral head and affects children between 3 and 11 years of age. It presents with pain in the hip or knee and causes a limp. All movements at the hip are limited.
- + Osteogenic sarcoma is predominantly a tumour of childhood or early adult life. The commonest sites are the lower end of the femur, the upper end of the tibia and the upper end of the humerus. Local pain and swelling are characteristic clinical features. Movements are usually not affected in the early stages.



A 65-year-old woman with a past medical history of osteoarthritis (only affecting her hand joints) and diet-controlled diabetes mellitus complains of a sudden onset of pain, swelling and stiffness in her right knee. Examination shows that the right knee is swollen, erythematous and tender.

Which one of the following tests is most likely to lead to a diagnosis?

- |   |  |
|---|--|
| A | X-ray of the knee                                |
| B | Autoimmune screen                                |
| C | Serum uric acid level                            |
| D | Aspiration and examination of the synovial fluid |
| E | A trial of colchicine                            |

- |   |  |
|---|--|
| A | X-ray of the knee                                |
| B | Autoimmune screen                                |
| C | Serum uric acid level                            |
| D | Aspiration and examination of the synovial fluid |
| E | A trial of colchicine                            |

## Explanation

### Synovial fluid examination

This woman may have a septic arthritis or pseudogout. The most appropriate test to lead to an early diagnosis is aspiration of the joint and examination of the synovial fluid under polarised light for rhomboid crystals that exhibit weakly positive birefringence, which is typical of pseudogout. A synovial fluid white cell count greater than  $50,000/\text{mm}^3$  with more than 90% neutrophils is highly suggestive of bacterial infection and Gram-stain examination and culture may reveal the organism responsible.

A 60-year-old diabetic woman with chronic arthritis has a swollen, red-hot and painful right knee following an intra-articular injection of steroid for pain relief 4 days earlier.

What test would confirm the diagnosis?

- |   |   |
|---|---|
| A | Urgent blood sugar estimation                         |
| B | Blood culture   |
| C | Joint aspiration and culture                          |
| D | Joint aspiration and microscopy under polarised light |
| E | Serum rheumatoid factor estimation                    |

- |   |   |
|---|---|
| A | Urgent blood sugar estimation                         |
| B | Blood culture   |
| C | Joint aspiration and culture                          |
| D | Joint aspiration and microscopy under polarised light |
| E | Serum rheumatoid factor estimation                    |

## Explanation

### Acute septic arthritis

This woman has developed acute septic arthritis following her intra-articular injection. Joint aspiration and culture would reveal the causative organisms, which are usually streptococci or staphylococci. After joint aspiration, empirical antibiotic therapy should be started with intravenous benzylpenicillin and flucloxacillin. Blood cultures may be negative as there is no evidence of septicaemia.



A 78-year-old man presents with an acute onset of severe pain and swelling of the left wrist, which had developed after he had a chest infection 2 weeks previously. On examination, he has a temperature of 38 °C and the left wrist is red, swollen and painful.

What is the most appropriate initial investigation?

A Erythrocyte sedimentation rate

B Full blood count

C Joint aspiration

D Serum urate concentration

E Radiography of the joint

A	Erythrocyte sedimentation rate
B	Full blood count
C	Joint aspiration
D	Serum urate concentration
E	Radiography of the joint

## Explanation

### Infective arthritis

The history of recent respiratory tract infection raises the possibility that this is an infective arthritis.

#### Causes

The most common cause of septic arthritis is *Staphylococcus aureus*, although seeding from respiratory infections caused by streptococci can also occur. Other causative organisms, such as *Neisseria gonorrhoeae* and *Haemophilus influenzae*, can cause septic arthritis in children. Opportunistic pathogens such as *Salmonella* may be responsible in sickle cell disease.

#### Management

Joint aspiration is essential and fluid should be sent for urgent Gram stain and culture. Treatment with antibiotics should begin immediately, as waiting for investigation reports can result in permanent joint destruction. Formal surgical toilet is required where there is evidence of osteomyelitis.

A 42-year-old woman with systemic lupus erythematosus (SLE) is attending the Rheumatology Clinic. She complains of shortness of breath.

Assuming that this is due to respiratory involvement by SLE, what would be the most common pulmonary manifestation?

- |   |                          |
|---|--------------------------|
| A | Pneumonitis              |
| B | Pleural effusion         |
| C | Atelectasis              |
| D | Restrictive lung disease |
| E | Pulmonary fibrosis       |

A	Pneumonitis
B	Pleural effusion
C	Atelectasis
D	Restrictive lung disease
E	Pulmonary fibrosis

## Explanation

### Pulmonary involvement in SLE

Recurrent pleurisy and pleural effusions are the most common manifestations of systemic lupus erythematosus (SLE) and are often bilateral. Pneumonitis and atelectasis may be seen; eventually a restrictive lung defect develops. Pulmonary fibrosis is rare.



A 70-year-old sheep farmer presents complaining of pain and restricted movements of his right hip for over a year. He also complains of early morning stiffness in the joint that lasts for about half an hour. The stiffness and pain have been progressively increasing and now he finds it difficult to carry out his routine activities. On examination he appears physically fit. An X-ray of the hip shows some decrease in joint space and subchondral sclerosis.

What is the most likely diagnosis?

- |   |                      |
|---|----------------------|
| A | Osteoarthritis       |
| B | Lyme disease         |
| C | Brucellosis          |
| D | Rheumatoid arthritis |
| E | Gouty arthritis      |

A	Osteoarthritis
B	Lyme disease
C	Brucellosis
D	Rheumatoid arthritis
E	Gouty arthritis

# Explanation

## Chronic joint pain

- + Osteoarthritis is the commonest joint condition in people of this age. Pain on movement, worse at the end of the day, and joint stiffness are characteristic features.
- + Lyme disease usually begins with erythema chronicum migrans. This may be associated with systemic malaise, including arthralgia, neck stiffness and lymphadenopathy. Weeks or months later, patients can develop meningoencephalitis, polyneuropathies, conduction disorders and myocarditis.
- + Brucellosis may present as pyrexia of unknown origin or with non-specific attacks of lassitude, headache, generalised myalgia and night sweats. Untreated brucellosis for a year or more can also present with bouts of depression. Splenomegaly is usually present, along with lymphadenopathy, arthritis and endocarditis. Arthralgia can occur but is not localised to a single joint and movements are not restricted.
- + Rheumatoid arthritis affects the peripheral small joints of the hands and feet and is usually symmetrical. Acute gouty arthritis usually affects the metatarsophalangeal joint.
- + The clinical picture does not support a diagnosis of acute gouty arthritis.

A young man presents to the Emergency Department with an acutely swollen and painful right knee, associated with red gritty eyes and dysuria. He has recently returned from Thailand, where he had diarrhoea and vomiting for several days. Joint aspiration shows the presence of giant macrophages. No organisms are seen on Gram staining.

What could the diagnosis be?

- |   |                      |
|---|----------------------|
| A | Reactive arthritis   |
| B | Behçet's disease     |
| C | Sjögren's syndrome   |
| D | Gonococcal arthritis |
| E | Septic arthritis     |



## Explanation

### Reactive arthritis (formerly Reiter syndrome)

This patient has the classic triad of reactive arthritis:

- + Arthritis
- + Conjunctivitis
- + Bacterial dysentery (although the condition of course also occurs after non-specific urethritis)

The condition is usually associated with HLA B27. The arthritis is of the reactive type, occurring after bacterial dysentery caused by *Salmonella*, *Shigella*, *Campylobacter* or *Yersinia* spp. or may follow sexually acquired infection with *Chlamydia* spp. Joint aspiration shows the presence of giant macrophages (Reiter's cells).

### Differential diagnosis

Septic arthritis presents as a red-hot swollen joint. Haematogenous spread from either the skin or upper respiratory tract is the most common mode of entry. The most likely organism in adults is *Staphylococcus aureus*. In younger sexually active patients, disseminated gonococcal infection is an important cause, which occurs in up to 3% of untreated gonorrhoea.

A 45-year-old woman presents with a 4-month history of malaise, weight loss, occasional fever and progressive difficulty in climbing stairs. On examination there is wasting of the pelvic girdle muscles with weakness. Blood test results are unremarkable except for raised anti-Jo-1 antibodies. Electromyography (EMG) shows spontaneous fibrillation, high-frequency repetitive potentials and polyphasic potentials on voluntary movements.

What is the most likely diagnosis?

- |   |                           |
|---|---------------------------|
| A | Polymyalgia rheumatica    |
| B | Osteoarthritis of the hip |
| C | Fibromyalgia              |
| D | Polymyositis              |
| E | Guillain-Barré syndrome   |

## Explanation

### Polymyositis

The history and findings are suggestive of adult polymyositis. This condition affects women three times more often than men. The onset can be insidious over several months. The major clinical feature is proximal muscle weakness, which is progressive. Wasting of the muscles might also be noted. Respiratory muscles are affected in severe disease (especially those patients with anti-Jo-1 antibodies).

### Investigations

The electromyogram (EMG) shows a typical triad of changes: spontaneous fibrillation potentials at rest, polyphasic or short-duration potentials on voluntary contraction, and salvos of repetitive potentials on mechanical stimulation of the nerve. A fine-needle muscle biopsy shows fibre necrosis and regeneration in association with an inflammatory cell infiltrate with lymphocytes around the blood vessels and between muscle fibres.

A 45-year-old woman with long-standing rheumatoid arthritis develops pain in her left knee. What is the earliest radiological evidence of rheumatoid arthritis of the knee?

- |   |                               |
|---|-------------------------------|
| A | Erosion of cartilage and bone |
| B | Loss of joint space           |
| C | Varus/valgus deformity        |
| D | Signs of an effusion          |
| E | Osteophyte formation          |



- |   |                               |
|---|-------------------------------|
| A | Erosion of cartilage and bone |
| B | Loss of joint space           |
| C | Varus/valgus deformity        |
| D | Signs of an effusion          |
| E | Osteophyte formation          |

## Explanation

### Rheumatoid arthritis in the knee

Massive synovitis and knee effusions are often the first evidence of rheumatoid arthritis of the knees. Osteophyte formation is a late occurrence and is caused by secondary osteoarthritis. Erosion of cartilage and bone and loss of joint space may lead to a valgus or varus deformity.

A 27-year-old woman is referred to the Rheumatology Clinic by her gynaecologist with a history of swelling and pain in her right big toe and left knee. The only positive finding on gynaecological examination was the presence of cervicitis. An endocervical swab tested positive for chlamydial infection.

What is the most probable diagnosis in this case?

A	Acute gouty arthritis
B	Rheumatoid arthritis
C	Reactive arthritis
D	Staphylococcal arthritis
E	Gonococcal arthritis

## Explanation

### Reactive arthritis

This woman has reactive arthritis triggered by *Chlamydia trachomatis*, causing non-specific cervicitis. Seronegative spondyloarthritis develops in 1-2% of patients with this condition.

### Differential diagnosis

- + Gout is more common in men in this age group and seldom occurs in premenopausal women.
- + Rheumatoid arthritis is a progressive, symmetrical peripheral polyarthritis affecting the small joints of the hands and feet.
- + Septic arthritis presents acutely with a red, hot, swollen and painful joint with restricted movements. The patient would be more likely to attend the Rheumatology Clinic first before seeing her gynaecologist.
- + There is no evidence to suggest gonococcal infection.

A 65-year-old woman, who lives alone, complains of increasing pain in her left knee. She finds it difficult to climb stairs and is on maximal paracetamol. Valgus deformity with obvious instability is also noted. Her knee radiograph shows osteoarthritis. Her body mass index (BMI) is 23 kg/m<sup>2</sup>.

What would be the treatment of choice for this patient?

- |   |                                     |
|---|-------------------------------------|
| A | Oral NSAIDs                         |
| B | Oral NSAIDs with gastric protection |
| C | Arthrodesis of the knee joint       |
| D | Joint replacement                   |
| E | Weight loss and physiotherapy       |



# Explanation

## Joint replacement

Joint replacement would be an effective treatment for this woman. Analgesia with non-steroidal anti-inflammatory drugs (NSAIDs) will provide only temporary relief, while arthrodesis would restrict her mobility even further.

Body mass index = weight in kg/(height in metres)<sup>2</sup>

A normal body mass index (BMI) is between 20 kg/m<sup>2</sup> and 25 kg/m<sup>2</sup>. This woman's weight is quite appropriate for her height, hence weight loss with physiotherapy would be an inappropriate management of her condition.

An old woman has back pain radiating down both legs. The pain is aggravated by walking and is relieved when she stops and leans forwards. On examination, the straight leg-raising test is negative. Ankle jerks are absent.

What is the most probable cause of her pain?

- |   |                    |
|---|--------------------|
| A | Osteoporosis       |
| B | Spinal stenosis    |
| C | Osteoarthritis     |
| D | Disc prolapse      |
| E | Vertebral fracture |

# Explanation

## Spinal stenosis

Symptoms of spinal stenosis occur as a result of limitation of space in the vertebral canal. This is a disorder of old age and commonly presents with pseudoclaudication, ie discomfort or pain in the legs on walking that is relieved by rest and by bending forwards. The diagnosis is confirmed by computed tomography or magnetic resonance imaging. Decompression is indicated if mobility or quality of life is significantly impaired.

A 49-year-old man who works in a plant assembling small- to medium-sized machine tools presents to the clinic complaining of pain on wrist extension. He says that the problem is getting worse at work and he is unable to grip well and carry the pieces of machinery he has assembled. On examination his blood pressure is 142/83 mmHg and his body mass index (BMI) is 26 kg/m<sup>2</sup>. General physical examination is unremarkable. The lateral elbow and forearm pain is reproduced when you ask him to perform resisted wrist extension. The maximal point of pain is about 0.5 to 1 cm distal to the lateral epicondyle.

Which one of the following is the most likely diagnosis?

A	Medial epicondylitis
B	Lateral epicondylitis
C	De Quervain's tenosynovitis
D	Carpal tunnel syndrome
E	Pronator syndrome



# Explanation

## Lateral epicondylitis

This man's symptoms are typical of lateral epicondylitis, also known as tennis elbow. Work-related lateral epicondylitis risk factors were identified in a systematic review, including the handling of tools greater in weight than 1 kg, regularly lifting loads greater than 20 kg a number of times in the day, and doing more than 2 hours of repetitive movements during any 1 day's work. Physiotherapy with the wearing of an elbow strap orthosis and local corticosteroid injections are effective treatment, as is a lateral release procedure in resistant cases.

A 55-year-old man presents with an acute myocardial infarction. He has been resuscitated and thrombolysed. He now mentions he has been feeling unwell for the last 2 months with dyspnoea, malaise, joint pains, weight loss and intermittent fever. His doctor has recently started him on an antihypertensive drug and he has recently experienced palpitations. He also gives a history of patchy numbness over his lower limbs and arms.

His blood tests reveal that he has a mildly raised urea and creatinine levels; his erythrocyte sedimentation rate (ESR) is 88 mm in 1st hour. There is no past history of intravenous drug abuse or of unprotected sex.

What is the diagnosis?

- |   |                            |
|---|----------------------------|
| A | Polymyalgia rheumatica     |
| B | Wegener's granulomatosis   |
| C | Polyarteritis nodosa (PAN) |
| D | Rheumatoid arthritis       |
| E | Occult malignancy          |

## Explanation

### Polyarteritis nodosa

This patient has multisystem involvement. Polyarteritis nodosa (PAN) is associated with hepatitis B antigenaemia and is a vasculitis secondary to the deposition of immune complexes. Renal impairment, hypertension, myocardial infarction, arrhythmias, heart failure and polyneuropathy are all known to occur. The diagnosis can be confirmed by histological examination of biopsy material from an affected organ, or by angiographic demonstration of microaneurysms in hepatic, intestinal or renal vessels.

A middle-aged man with red scaly patches on his elbows and knees presents with pain in the distal interphalangeal joints. You suspect psoriatic arthritis.

Which one of the following is most strongly linked in men to this condition?

- A Age of onset 20-30 years
- B Occurrence of arthropathy at the same time as the skin lesions
- C Minimal destruction of cartilage and bone
- D Involvement mainly of the distal interphalangeal joints
- E Occurrence of Bouchard's nodes in the proximal interphalangeal joints



- |   |   |
|---|---|
| A | Age of onset 20-30 years  |
| B | Occurrence of arthropathy at the same time as the skin lesions        |
| C | Minimal destruction of cartilage and bone                             |
| D | Involvement mainly of the distal interphalangeal joints               |
| E | Occurrence of Bouchard's nodes in the proximal interphalangeal joints |

## Explanation

### Psoriatic arthritis

The usual age of onset of psoriatic arthritis is 30-50 years - much later than the skin lesions. Cartilage and bone destruction may be unusually severe - arthritis mutilans.

Bouchard's nodes are seen in osteoarthritis.

DIPJ involvement occurs in 5-10% of patients with psoriatic arthritis, but in men is said to be a 'classical' feature of the disease.

A 55-year-old woman with a chronic disease develops nephrotic syndrome. She undergoes a renal biopsy to establish a diagnosis. On light microscopy, eosinophilic deposits are seen in the mesangium, capillary loops and arteriolar walls. Staining with Congo red renders these deposits pink and they show green birefringence under polarised light.

With which chronic disease is this condition most commonly associated?

A	Ulcerative colitis
B	Bronchiectasis
C	Rheumatoid arthritis
D	Osteoarthritis
E	Crohn's disease

A Ulcerative colitis

B Bronchiectasis

C Rheumatoid arthritis

D Osteoarthritis

E Crohn's disease

## Explanation

### Causes of secondary amyloidosis

The microscopic features are highly suggestive of amyloidosis. This patient most probably has secondary amyloidosis caused by her chronic disease. Rheumatoid arthritis is the most common cause of secondary amyloidosis. In developing countries it may be associated with infectious diseases such as tuberculosis, bronchiectasis and osteomyelitis.

A 27-year-old woman who works as a choreographer has rheumatoid arthritis of her hands. She is worried that it may spread to her feet.

What is the earliest manifestation of rheumatoid arthritis in the feet?

A Swelling of the metatarsophalangeal joints

B Broadening of the foot

C Loss of flexibility of the foot

D Flattening of the medial arch

E Valgus position of the ankle



A	Swelling of the metatarsophalangeal joints
B	Broadening of the foot
C	Loss of flexibility of the foot
D	Flattening of the medial arch
E	Valgus position of the ankle

## Explanation

### Rheumatoid arthritis in the foot

Painful swelling of the metatarsophalangeal joints is an early manifestation of rheumatoid arthritis. The foot then becomes broader and a hammer-toe deformity develops. Mid- and hind-foot rheumatoid arthritis causes a flat medial arch and loss of flexibility of the foot.

A 30-year-old salesman recently returned from Thailand complaining of redness in his eyes and a swollen knee joint. He says he had dysentery 4 weeks earlier, for which he received a course of antibiotics. There is no history of dysuria and a routine urine examination is normal.

What additional assessment would be most likely to provide contributory information for making a diagnosis?

- |   |                                  |
|---|----------------------------------|
| A | Joint aspiration and culture     |
| B | Blood culture                    |
| C | Auscultation of the chest        |
| D | Culture of urethral discharge    |
| E | History and physical examination |

- |   |                                  |
|---|----------------------------------|
| A | Joint aspiration and culture     |
| B | Blood culture                    |
| C | Auscultation of the chest        |
| D | Culture of urethral discharge    |
| E | History and physical examination |

## Explanation

### Reactive arthritis

This patient has reactive arthritis. Diagnosis of this condition is usually made from history and examination. Arthritis and conjunctivitis may follow 4–6 weeks after genitourinary (chlamydial) or gastrointestinal (*Shigella*, *Yersinia*) infection. The arthritis is typically an acute, asymmetrical, lower-limb arthritis. No positive results will be obtained from joint aspirates and blood cultures in reactive arthritis. A normal urinalysis rules out urethritis and the urethral discharge will be sterile.

An 11-year-old Asian girl presents with a 2-week history of fever, joint pains, malaise and loss of appetite. Swelling, redness and pain occurred in the left knee, lasted for 3 days, and then settled. The joint symptoms were preceded by an episode of pharyngitis. This was followed by swelling, redness and pain in her left elbow for 4 days, followed by similar symptoms in her right knee. At present she has a swollen, tender right ankle. No other abnormality is found on clinical examination.

What is the most likely diagnosis?

- |   |   |
|---|---|
| A | Still's disease                             |
| B | Rheumatic fever                             |
| C | Polyarticular juvenile idiopathic arthritis |
| D | Childhood dermatomyositis                   |
| E | Familial Mediterranean fever                |



# Explanation

## Rheumatic fever

Rheumatic fever predominantly affects children aged 4–15 years as a result of a Group A streptococcal infection. It is common in the Middle East, the Far East, Asia, Eastern Europe and South America. The arthritis is classically a fleeting migratory polyarthritis affecting the large joints. Isolated arthritis is the presenting symptom in 15–40% of cases of rheumatic fever, however.

## Differential diagnosis:

- + In Still's disease, the arthritis is usually much more persistent in each affected joint.
- + In polyarticular juvenile idiopathic arthritis, small joints are initially involved and fever does not occur.
- + Childhood dermatomyositis affects children between 4 and 10 years of age. The typical rash of dermatomyositis is usually accompanied by muscle weakness. Fever and joint pains do not usually occur.
- + Familial Mediterranean fever is inherited as an autosomal recessive condition and occurs in certain ethnic groups (Arab, Turkish and Armenian populations and Sephardic Jews). It is characterised by recurrent attacks of fever, arthritis and serositis. Abdominal or chest pain due to peritonitis or pleurisy can occur.

A 66-year-old man who has a red, target-shaped rash on his leg, experiences fatigue, left arm pain and numbness and difficulty using his left hand for gripping. He has also developed pain and swelling of his right wrist and left knee.

Which investigation would be most likely to help in making a diagnosis?

- |   |  |
|---|--|
| A | CRP estimation                                 |
| B | Blood culture                                  |
| C | Skin biopsy                                    |
| D | Antibody titre for <i>Borrelia burgdorferi</i> |
| E | Test for rheumatoid factor                     |

A	CRP estimation
B	Blood culture
C	Skin biopsy
D	Antibody titre for <i>Borrelia burgdorferi</i>
E	Test for rheumatoid factor

## Explanation

### Lyme disease

This man has Lyme disease. The causative organism is *Borrelia burgdorferi*, which is tick-borne. It usually begins with erythema chronicum migrans. This starts as a small papule, developing into a slowly enlarging red ring with a raised border. It fades from the centre. Malaise, arthralgia, neck stiffness and lymphadenopathy may occur. Diagnosis is serological. These patients test negative for rheumatoid factor. The other tests would not provide a conclusive diagnosis.

A 35-year-old man presents with a painful, swollen left knee, swollen ankles and right hallux, acutely inflamed eyes and dysuria. He was previously well, except for an episode of gastroenteritis 2 weeks previously. Clinical examination also reveals a left Achilles tendinitis and right plantar fasciitis. Radiography demonstrates left sacroiliitis, with evidence of enthesopathy, erosions and fluffy periostitis. He is HLA-B27-positive.

What is the most likely diagnosis?

- |   |  |
|---|--|
| A | Ankylosing spondylitis                               |
| B | Arthritis associated with inflammatory bowel disease |
| C | Gonococcal arthritis                                 |
| D | Reactive arthritis                                   |
| E | Sero-negative rheumatoid arthritis                   |



## Explanation

### Reactive arthritis (formerly Reiter syndrome)

This clinical scenario satisfies the diagnostic criteria for reactive arthritis – arthritis, conjunctivitis and urethritis following an episode of infective dysentery. The radiographic findings are characteristic for a reactive arthritis. Reactive arthritis occurs predominantly in men, most frequently in the third decade. There is a strong association with HLA B27 (63–96% of patients depending on case series).

Treatment in the acute stage is with non-steroidal anti-inflammatory agents. Reactive arthritis can also be associated with *Chlamydia trachomatis* and where there are associated urinary symptoms antibiotics should be prescribed as well as non-steroidal anti-inflammatory drugs (NSAIDs).

A business executive presents with a red-hot, swollen and very painful right big toe. Joint aspiration reveals no organisms but there are numerous neutrophils containing long, needle-shaped crystals.

What is the probable diagnosis?

- |   |                      |
|---|----------------------|
| A | Septic arthritis     |
| B | Gouty arthritis      |
| C | Rheumatoid arthritis |
| D | Gonococcal arthritis |
| E | Reiter syndrome      |

- |   |                      |
|---|----------------------|
| A | Septic arthritis     |
| B | Gouty arthritis      |
| C | Rheumatoid arthritis |
| D | Gonococcal arthritis |
| E | Reiter syndrome      |

## Explanation

### Acute gout

The synovial fluid in cases of acute gout shows increased turbidity as a result of the greatly elevated cell count ( $> 90\%$  neutrophils). Long, needle-shaped crystals are seen in the synovial fluid and within neutrophils. These crystals are negatively birefringent when seen under polarised light.

### Differential diagnosis

- + Joint aspiration in septic arthritis shows organisms in only 50% of cases. Crystals are not seen.
- + Reiter syndrome is a classic triad of non-specific urethritis, conjunctivitis and reactive arthritis. It is predominantly a disease of young men, with a male to female ratio of 15:1.
- + Rheumatoid arthritis usually affects multiple joints symmetrically. Erythema is not a feature.

A 25-year-old mechanic complains of stiffness and low back pain that is worse in the mornings. He is HLA B27-positive. A provisional diagnosis of ankylosing spondylitis is made.

What would be the most characteristic finding on an X-ray of the lower spine?

- |   |   |
|---|---|
| A | Narrowing of disc space   |
| B | Subchondral bony sclerosis on the iliac sides of the sacro iliac joints |
| C | Osteophyte formation  |
| D | Spondylolisthesis   |
| E | Osteoporosis of trabecular bone   |



- |   |   |
|---|---|
| A | Narrowing of disc space   |
| B | Subchondral bony sclerosis on the iliac sides of the sacro iliac joints |
| C | Osteophyte formation  |
| D | Spondylolisthesis   |
| E | Osteoporosis of trabecular bone   |

## Explanation

### X-ray changes in ankylosing spondylitis

The X-ray in early ankylosing spondylitis may show subchondral bony sclerosis on the iliac sides of the sacroiliac joints. Narrowing of the disc space is typically seen in patients with a prolapsed intervertebral disc. Spondylolisthesis is slippage of one vertebral body over another as seen on X-ray. Osteophyte formation (syndesmophytes) occurs later and may cause bony ankylosis and permanent stiffening.

A 79-year-old woman who drinks 30 units of alcohol per week presents with a red, hot swollen ankle.

Which of the following investigations is most useful with respect to confirming a definitive diagnosis?

- |   |                                 |
|---|---------------------------------|
| A | Blood culture                   |
| B | Joint aspiration and microscopy |
| C | Joint aspiration and culture    |
| D | X-ray of the ankle              |
| E | Serum uric acid levels          |

A	Blood culture
B	Joint aspiration and microscopy
C	Joint aspiration and culture
D	X-ray of the ankle
E	Serum uric acid levels

## Explanation

### Diagnosis of acute gouty arthritis

This patient most probably has acute gouty arthritis that may be precipitated by her high alcohol intake. Joint aspiration and microscopy can show the characteristic long, needle-shaped crystals (uric acid crystals) that are negatively birefringent under polarised light. Serum uric acid levels may actually be low in cases of acute gout.

Septic arthritis is rare in the absence of any systemic infection or injury to the joint.

A 57-year-old woman with rheumatoid arthritis has been attending the Rheumatology Clinic for several years. You are reviewing her case notes in order to summarise her case for referral to a colleague.

While the presentation and progression of rheumatoid arthritis is variable, what is the most common form or course of this condition?

- A Palindromic
- B Transient
- C Remitting
- D Chronic and persistent
- E Rapidly progressive



- |   |                        |
|---|------------------------|
| A | Palindromic            |
| B | Transient              |
| C | Remitting              |
| D | Chronic and persistent |
| E | Rapidly progressive    |

## Explanation

### Forms of rheumatoid arthritis

- + The most typical form of rheumatoid arthritis is the chronic persistent type. The disease follows a relapsing and remitting course over many years.
- + Monoarticular attacks lasting 24-48 hours are called 'palindromic'.
- + In the transient type, the disease is self-limiting, lasting < 12 months and leaving no permanent joint damage.
- + The remitting type is associated with active arthritis for several years that then remits, leaving minimal damage.
- + Severe joint damage and disability occur in the rapidly progressive type.

A 27-year-old man complains of low back pain for some years. He says he had an episode of severe diarrhoea 3 weeks earlier, and that he has experienced waxing and waning stomach problems that have gone on for a couple of years. An X-ray of the lumbosacral spine shows erosion of the lower joint margins of the vertebrae.

What is the probable diagnosis?

- |   |                        |
|---|------------------------|
| A | Ankylosing spondylitis |
| B | Reactive arthritis     |
| C | Gonococcal arthritis   |
| D | Lumbar disc prolapse   |
| E | Osteoarthritis         |

# Explanation

## Ankylosing spondylitis

This patient has ankylosing spondylitis (AS). The main lesion is spinal ankylosis with sacroiliac joint involvement. X-ray of the sacroiliac joints might show squaring of the vertebrae, erosions of the apophyseal joints and obliteration of the sacroiliac joints. It may be precipitated by an infection (eg with *Yersinia*) in genetically predisposed individuals (HLA-B27 gene).

## Differential diagnosis

- + Reactive arthritis is a triad of arthritis, urethritis and conjunctivitis that follows 4-6 weeks after a genitourinary (chlamydial) or gastrointestinal (*Shigella*, *Yersinia*, *Campylobacter*) infection.
- + Restricted forward flexion with pain radiating into the buttocks or down the legs (sciatica) characterises lumbar disc prolapse.
- + Osteoarthritis is usually a degenerative disease of older age (> 55 years). Osteophytes may be seen in the intervertebral joints in osteoarthritis and the disc space might be narrowed.

A 74-year-old man has an acutely painful, red and swollen knee. He is suffering from congestive cardiac failure, chronic renal impairment and is currently on digoxin and furosemide. A most recent creatinine was measured at 135 micromol/l. CRP is slightly elevated and white cell count is normal.

What treatment would be most appropriate for his joint pain?

- |   |             |
|---|-------------|
| A | Aspirin     |
| B | Paracetamol |
| C | Colchicine  |
| D | Diclofenac  |
| E | Indometacin |



- |   |             |
|---|-------------|
| A | Aspirin     |
| B | Paracetamol |
| C | Colchicine  |
| D | Diclofenac  |
| E | Indometacin |

## Explanation

Gout precipitated by diuretic therapy

Given his history of congestive cardiac failure, it would seem most appropriate to manage his acute gout with colchicine. This is associated with less gastrointestinal irritation than NSAIDs and is not associated with fluid retention.

You review a 21-year-old man who suffered from Still's disease as a child. Which one of the following are common features of Still's disease?

- |   |   |
|---|---|
| A | Negative rheumatoid factor                  |
| B | Normal erythrocyte sedimentation rate (ESR) |
| C | Normal C-reactive protein (CRP)             |
| D | Thrombocytopenia                            |
| E | Splenic atrophy                             |

A	Negative rheumatoid factor
B	Normal erythrocyte sedimentation rate (ESR)
C	Normal C-reactive protein (CRP)
D	Thrombocytopenia
E	Splenic atrophy

## Explanation

### Still's disease

Still's disease (which accounts for 10% of cases of juvenile idiopathic arthritis or JIA) affects boys and girls equally up to the age of 5 years; after this point, girls are more commonly affected. Adult-onset Still's disease is rare. Clinical features include fever, maculopapular rash, myalgia and generalised lymphadenopathy. Hepatosplenomegaly, pericarditis and pleurisy also occur. Laboratory tests reveal raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), neutrophilia and thrombocytosis, though autoantibodies are negative.

A 44-year-old woman complains of tiredness and lower limb joint pains.

Which one of the following joint findings is most suggestive of an inflammatory rather than an osteoarthritic cause of joint pain?

- |   |                            |
|---|----------------------------|
| A | Swelling and warmth        |
| B | Crepitus                   |
| C | Bony articular enlargement |
| D | Instability                |
| E | Painful range of motion    |



A	Swelling and warmth
B	Crepitus
C	Bony articular enlargement
D	Instability
E	Painful range of motion

## Explanation

### Inflammatory arthritis vs osteoarthritis

- + A swollen and warm joint is more likely to be affected by an inflammatory arthritis than by osteoarthritis.
- + The presence of synovial fluid is more commonly associated with inflammatory arthritis than with osteoarthritis.
- + Warmth suggests some degree of inflammation.
- + Osteoarthritis is typically associated with bony joint enlargement in response to cartilage and subchondral bone injury.
- + Painful joint movement, joint crepitus and joint instability can occur in both an inflammatory and an osteoarthritic joint.

A 30-year-old woman with long-standing Raynaud's phenomenon develops tightness and swelling of her fingers associated with tightness around her mouth. Blood tests show: haemoglobin 10.1 g/dl and mean corpuscular volume (MCV) 87 fl. Anticentromere antibodies are positive.

What is the probable diagnosis?

A Systemic lupus erythematosus

B Primary Sjögren syndrome

C Systemic sclerosis

D Polymyalgia rheumatica

E Polymyositis

# Explanation

## Systemic sclerosis

Systemic sclerosis can be classified by the presence of limited or diffuse disease.

### Limited cutaneous systemic sclerosis

This was formerly called the CREST syndrome (calcinosis, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly and telangiectasia). It is characterised by the early development of Raynaud's phenomenon many years before the onset of skin changes. The immune marker of this disease is the anticentromere antibody.

### Diffuse cutaneous systemic sclerosis

Here the skin changes develop earlier and are associated with earlier pulmonary and renal disease. These can be accompanied by gastrointestinal and cardiac involvement. The presence of anti-Scl antibody (in 30% of cases) is characteristic.

A 23-year-old man with seropositive rheumatoid arthritis is planning to start a family. Which one of the following drugs would be safest to prescribe to help control his disease?

- |   |                  |
|---|------------------|
| A | Sulfasalazine    |
| B | Methotrexate     |
| C | Leflunomide      |
| D | Prednisolone     |
| E | Cyclophosphamide |



A 23-year-old man with seropositive rheumatoid arthritis is planning to start a family. Which one of the following drugs would be safest to prescribe to help control his disease?

A	Sulfasalazine
B	Methotrexate
C	Leflunomide
D	Prednisolone
E	Cyclophosphamide

## Explanation

### Anti-rheumatoid drugs and fertility

Sulfasalazine causes a transient aspermia and cyclophosphamide may irreversibly affect male fertility. Methotrexate and leflunomide both inhibit purine/pyrimidine synthesis (the former by inhibiting folate metabolism) and are contraindicated in pregnancy or while trying to conceive. Prednisolone, while having many other unwanted side-effects, is a relatively safe agent to use for short periods of time.

A 63-year-old man from Ghana presents with backache, lethargy and thirst. His erythrocyte sedimentation rate (ESR) is raised with normocytic normochromic anaemia.

What is the most likely diagnosis?

- A Multiple myeloma
- B Osteoporosis
- C Osteoarthritis
- D Paget's disease of bone
- E Calcium pyrophosphate arthropathy

# Explanation

## Multiple myeloma

Multiple myeloma is a malignant proliferation of plasma cells. It is more common in Afro-Caribbeans. Lytic lesions in the bones cause bone pain, fractures and hypercalcaemia, which results in lethargy and thirst.

Differential diagnosis:

- + Paget's disease classically presents with bone pain, bone deformity, deafness and pathological fractures.
- + Calcium pyrophosphate arthropathy (CPA) or chondrocalcinosis particularly targets the knee joint. Anaemia is not a feature.
- + Anaemia is not a feature of CPA or osteoarthritis.
- + Osteoporosis is rare in men at this age unless associated with hypogonadism. Again, anaemia and a raised erythrocyte sedimentation rate (ESR) are not seen in osteoporosis.

A 31-year-old woman complains of pain in the fingers of both hands.

Which additional clinical and/or immunological finding would be most likely to be found if rheumatoid arthritis is suspected?

A Subcutaneous nodules

B Antinuclear antibodies

C Rheumatoid factor

D Crepitus

E Entrapment neuropathy



A Subcutaneous nodules

B Antinuclear antibodies

**C Rheumatoid factor**

D Crepitus

E Entrapment neuropathy

## Explanation

### Early signs of rheumatoid arthritis

Rheumatoid factor is found in 70% of patients with rheumatoid arthritis. Subcutaneous nodules occur in 25%, while antinuclear antibodies are seen in 30% of cases. Entrapment neuropathy (eg carpal tunnel syndrome) is less common but is known to occur in cases of rheumatoid arthritis.

Crepitus is a characteristic finding in osteoarthritis.

A 34-year-old woman with long-standing rheumatoid arthritis is found to have anaemia. Blood tests show: haemoglobin 10.5 g/dl (normal range 11.5–16.5 g/dl), mean cell haemoglobin (MCH) 30 pg (28–32 pg), mean cell haemoglobin concentration (MCHC) 37 g/dl (32–35 g/dl), mean corpuscular volume (MCV) 94 fl (80–96 fl), white cell count (WCC)  $7.5 \times 10^9/l$  ( $4-11 \times 10^9/l$ ) and platelets  $175 \times 10^9/l$  ( $150-400 \times 10^9/l$ ).

What is the most common cause for this condition?

- |   |  |
|---|--|
| A | Non-steroidal anti-inflammatory drug (NSAID) ingestion   |
| B | Felty syndrome   |
| C | Chronic disease  |
| D | Disease-modifying anti-rheumatoid drug (DMARD) treatment |
| E | Haemolytic anaemia                                       |

- |   |  |
|---|--|
| A | Non-steroidal anti-inflammatory drug (NSAID) ingestion   |
| B | Felty syndrome   |
| C | Chronic disease  |
| D | Disease-modifying anti-rheumatoid drug (DMARD) treatment |
| E | Haemolytic anaemia                                       |

## Explanation

### Anaemia in rheumatoid arthritis

- + Anaemia in patients with rheumatoid arthritis is usually the normocytic normochromic anaemia of chronic disease.
- + Iron deficiency can occur as a result of gastrointestinal blood loss from non-steroidal anti-inflammatory drug (NSAID) ingestion or haemolytic (Coombs'-positive) anaemia.
- + Pancytopenia occurs in Felty syndrome or as a complication of disease-modifying anti-rheumatoid drug (DMARD) treatment.

A 26-year-old woman presents with a malar rash, photosensitivity and arthralgia. On examination she has oral ulcers and her urine dipstick shows haematuria and proteinuria.

Given the suspected diagnosis, which antibody would be particularly specific for the disease?

- |   |                                    |
|---|------------------------------------|
| A | Antinuclear antibody               |
| B | Anti-dsDNA antibody                |
| C | Antimitochondrial antibody         |
| D | Rheumatoid factor                  |
| E | Nuclear U1 ribonucleoprotein (RNP) |



# Explanation

## Anti-dsDNA antibodies

Levels of antibody to double-stranded DNA (anti-dsDNA) are particularly useful. This test is virtually specific for systemic lupus erythematosus, especially if the immunoglobulins are of the IgG isotype. The anti-dsDNA result is usually quantified and this value is a measure of the activity of the disease.

- + Anti-U1 RNP antibodies are associated with mixed connective tissue disease
- + Many individuals are low titre antinuclear antibody positive, such that whilst it is associated with SLE, it isn't specific for the disorder
- + Antimitochondrial antibodies are associated with primary biliary cirrhosis

A 30-year-old man presents with malaise, fever, backache and joint pains of 1 week's duration. On examination, arthritis is present asymmetrically in the lower limbs, involving the knees, one ankle, and some metatarsophalangeal and toe joints. An eye examination reveals conjunctival congestion and there is a vesicular crusting lesion on his left sole. Investigations reveal: erythrocyte sedimentation rate (ESR) 60 mm in 1st hour, C-reactive protein (CRP) 50 mg/l; rheumatoid factor is negative and HLA B27 is positive.

Which one of the following is the most likely diagnosis?

- |   |                        |
|---|------------------------|
| A | Rheumatoid arthritis   |
| B | Gout                   |
| C | Reactive arthritis     |
| D | Psoriatic arthritis    |
| E | Ankylosing spondylitis |

# Explanation

## Reactive arthritis

The spondyloarthropathies share common clinical features and HLA B27 positivity. Rheumatoid factor is usually negative. This group of diseases includes:

- + Ankylosing spondylitis
- + Reactive arthritis (formerly known as Reiter syndrome)
- + Psoriatic arthritis
- + Enteropathic arthritis
- + Undifferentiated arthritis

## Clinical features of reactive arthritis

Patients with reactive arthritis may have had a prodromal infection 1-4 weeks before its onset, usually with *Shigella*, *Salmonella*, *Yersinia*, *Campylobacter* or *Chlamydia* spp. Constitutional symptoms and asymmetric lower limb arthritis are characteristic. Skin lesions include vesicular keratoderma blennorrhagica (usually on the palms and soles) and circinate balanitis on the glans penis.

## Differential diagnosis

- + Psoriatic arthritis is a close differential, but the arthritis is usually in the upper limb and more gradual in onset. The skin lesions in psoriasis are flat-topped plaques with silvery scales, usually found on the elbows, knees and scalp.
- + Rheumatoid arthritis usually presents with gradual-onset symmetrical arthritis.
- + Gout is usually acute and monoarticular.

A 62-year-old man presents to his GP for review. He has severe pain affecting the right shoulder which is worst during the middle range of abduction. He is unable to initiate abduction of his shoulder via active movement, although passive elevation is less painful. There are no other abnormal physical signs.

What diagnosis fits best with this clinical picture?

- |   |                                     |
|---|-------------------------------------|
| A | Torn rotator cuff                   |
| B | Subacromial bursitis                |
| C | Supraspinatus tendonitis            |
| D | Adhesive capsulitis                 |
| E | Acromio-clavicular joint disruption |



# Explanation

## Supraspinatus tendonitis

Supraspinatus tendonitis is one of the commonest causes of painful restriction of shoulder movement across all ages. In 30% of cases there is a definite history of trauma. Fewer than 5% of cases are bilateral. Pain radiates to the upper arm and is made worse by active abduction and elevation. Passive elevation reduces impingement of the tendon and is often less painful.

Supraspinatus muscle is the main one involved in the initial range of abduction, particularly the first 15°, and deltoid then predominates increasingly for the remainder of the range. Impaired initiation of abduction is therefore typically present.

## Management

Analgesics or non-steroidal anti-inflammatory drugs (NSAIDs) are the treatment of choice, although some patients may require local corticosteroid injection. Around 70% of patients improve without physiotherapy over a 5–20-day period. Physiotherapy may aid mobilisation in patients with persistent stiffness.

A 9-year-old girl presents with pain and swelling of the fingers of both hands and wrists. X-ray of the hands is normal. A blood test is positive for rheumatoid factor.

What is the most likely diagnosis?

- |   |   |
|---|---|
| A | Still's disease                             |
| B | Persistent oligoarthritis                   |
| C | Juvenile spondyloarthropathy                |
| D | Polyarticular juvenile idiopathic arthritis |
| E | Psoriatic arthritis                         |

# Explanation

## Polyarticular juvenile idiopathic arthritis

The rheumatoid factor-positive form of polyarticular juvenile idiopathic arthritis (JIA) occurs in older girls, usually aged over 8 years. The arthritis initially involves the small joints of the hands, wrists, ankles and feet.

### Differential diagnosis of arthralgia in children

- + Still's disease presents with a high-swinging early-evening pyrexia, a maculopapular rash with arthralgia and arthritis, myalgia and generalised lymphadenopathy.
- + Persistent oligoarthritis mainly affects girls, with a peak age incidence at 3 years. Uveitis is common in this condition.
- + Juvenile spondyloarthropathy affects teenage and younger boys, mainly manifest an asymmetric arthritis of the lower-limb joints and enthesitis.
- + Psoriatic arthritis in children is similar to the adult form. Skin lesions can develop long after the arthritis. Rheumatoid factor is negative in this condition.

A 57-year-old man presents with problems with cold, blue fingertips and a purpuric rash. His GP is also concerned because a recent faecal occult blood sample was reported as positive. Other significant history includes arthralgia affecting his knees, ankles, elbows and wrists. He has a history of hypertension, for which he takes enalapril. On examination he has a blood pressure of 155/85 mmHg. He has cold peripheries and palpable purpura on examination of his skin. There is evidence of joint swelling affecting his knees, wrists and the small joints of his fingers. Investigations reveal: haemoglobin, 12.1 g/dl, white cell count,  $8.9 \times 10^9/l$ , platelets,  $204 \times 10^9/l$ , sodium 138 mmol/l, potassium 4.9 mmol/l, creatinine 165  $\mu\text{mol/l}$ . Urinalysis shows blood ++, protein ++.

Given the suspected diagnosis, which one of the following blood tests is most likely to be positive?

- |   |                             |
|---|-----------------------------|
| A | Anti-nuclear antibody       |
| B | Rheumatoid factor           |
| C | c-ANCA                      |
| D | p-ANCA                      |
| E | Anti-smooth muscle antibody |



A	Anti-nuclear antibody
B	Rheumatoid factor
C	c-ANCA
D	p-ANCA
E	Anti-smooth muscle antibody

## Explanation

### Mixed cryoglobulinaemia

The symptoms, clinical examination and investigations described here are suggestive of mixed cryoglobulinaemia. Gastrointestinal bleeding, glomerulonephritis, palpable purpura and arthralgia are typical signs of type II or III cryoglobulinaemia. Both types are associated with the presence of IgM rheumatoid factor. Where there is evidence of end-organ damage as there is here, corticosteroids in conjunction with a second-line agent such as cyclophosphamide or azathioprine are the mainstay of therapy. Non-steroidal anti-inflammatory drugs may be useful in the management of arthralgia.

A 33-year-old Japanese man complains of recurrent oral and genital ulcers as well as painful nodules on his shins. In the past he has suffered from recurrent episodes of itchy and red eyes and thrombophlebitis in his legs.

What is the most likely diagnosis?

- |   |                              |
|---|------------------------------|
| A | Vasculitis                   |
| B | Behçet's syndrome            |
| C | Familial Mediterranean fever |
| D | Reactive arthritis           |
| E | Palindromic rheumatism       |

## Explanation

### Behçet syndrome

Behçet syndrome is commonly seen in natives of Japan and East Mediterranean countries. It is characterised by recurrent oral and genital ulcers, arthralgias, erythema nodosum, iritis and thrombophlebitis.

A 27-year-old woman has psoriatic arthritis.

Which one of the following hand conditions is most commonly associated with this disease?

- |   |                                    |
|---|------------------------------------|
| A | Cutaneous lesions                  |
| B | Tenosynovitis                      |
| C | Nail dystrophy                     |
| D | Proximal interphalangeal arthritis |
| E | Arthritis mutilans                 |



- |   |                                    |
|---|------------------------------------|
| A | Cutaneous lesions                  |
| B | Tenosynovitis                      |
| C | Nail dystrophy                     |
| D | Proximal interphalangeal arthritis |
| E | Arthritis mutilans                 |

## Explanation

### Psoriatic arthritis

Nail dystrophy (pitting, subungual hyperkeratosis and/or onycholysis) is most commonly seen in patients with psoriatic arthritis. Arthritis mutilans affects about 5% of patients with this disease. Classic psoriatic arthritis involves the distal interphalangeal joints. Cutaneous lesions may be mild or may develop after the arthritis.

A 65-year-old woman presents with a 1-month history of weakness in the hip region and inability to walk or get up from a chair. On examination there is wasting of the pelvic girdle muscles. She has also developed a purple discoloration of the eyelids. You suspect adult dermatomyositis.

Which one of the following investigations will be most helpful in the diagnosis and management of this condition?

- |   |                                     |
|---|-------------------------------------|
| A | A raised ESR                        |
| B | Presence of rheumatoid factor       |
| C | Presence of antinuclear antibody    |
| D | Myositis-specific antibodies        |
| E | Raised serum creatine phosphokinase |

A	A raised ESR
B	Presence of rheumatoid factor
C	Presence of antinuclear antibody
D	Myositis-specific antibodies
E	<b>Raised serum creatine phosphokinase</b>

## Explanation

### Investigation of dermatomyositis

Serum creatine phosphokinase, aminotransferases and aldolase are usually raised and are useful guides to the activity of the disease. A raised erythrocyte sedimentation rate (ESR) is a response to any inflammatory reaction in the body. In this condition, the ESR is raised in about 5% of cases. Antinuclear antibodies, myositis-specific antibodies and rheumatoid factor are not present in all cases of dermatomyositis and so are not helpful in the diagnosis or management of this condition.

A 35-year-old woman who suffers from rheumatoid arthritis attends the Rheumatology Clinic complaining of marked episodic pain in her right hand. Physical examination reveals a loss of pinprick sensation in the hand. There is tingling and numbness involving the thumb, index and middle fingers. You suspect median nerve compression.

Which one of the following clinical findings is most commonly associated with this condition?

A Wasting of the interosseous and hypothenar muscles

B Severe cubitus valgus

C Loss of sensation in the lateral palmar aspect

D Swelling on the back of the hand

E Positive Tinel's sign



- |   |  |
|---|--|
| A | Wasting of the interosseous and hypothenar muscles |
| B | Severe cubitus valgus                              |
| C | Loss of sensation in the lateral palmar aspect     |
| D | Swelling on the back of the hand                   |
| E | Positive Tinel's sign                              |

## Explanation

### Carpal tunnel syndrome

This woman most probably has carpal tunnel syndrome, which is due to compression of the median nerve as it passes under the flexor retinaculum. Pregnancy, the oral contraceptive pill, myxoedema and rheumatoid arthritis can all exacerbate compression. Tapping the median nerve in the carpal tunnel reproduces tingling and pain - known as Tinel's sign. Lateral palmar sensation is spared in carpal tunnel syndrome, as its supply, the palmar cutaneous branch of the median nerve, does not pass through the carpal tunnel.

### Differential diagnosis

Wasting of the interosseous and hypothenar muscles occurs in ulnar neuritis. This can occur following a childhood supracondylar fracture that results in severe cubitus valgus and consequent friction of the ulnar nerve. Swelling on the back of the hand and wrist occurs in dorsal tenosynovitis, which is usually associated with rheumatoid arthritis. This is not associated with symptoms of median nerve compression.

A 5-year-old girl complains of progressively increasing severe pain in her left hip and upper leg for the last week. She is able to walk with a limp. On examination there is extreme tenderness over the upper thigh. The hip joint is not swollen. Blood tests show: white cell count (WCC)  $18 \times 10^9/l$ , erythrocyte sedimentation rate (ESR) 87 mm in 1st hour and C-reactive protein (CRP) 110 mg/l. X-rays and ultrasound scans of the hip are normal.

What is the most probable diagnosis?

- |   |                      |
|---|----------------------|
| A | Osteomyelitis        |
| B | Septic arthritis     |
| C | Ewing's tumour       |
| D | Lumbar disc prolapse |
| E | Perthe's disease     |

## Explanation

### Osteomyelitis

This girl has osteomyelitis of the femur. X-ray changes are not apparent for a few days but then show haziness and loss of density of the affected bone followed by subperiosteal reaction and, later, sequestrum and involucrum. A hot, painful, swollen joint usually accompanies septic arthritis.

### Differential diagnosis

- + Ewing's tumour is a malignant sarcoma found most commonly in the diaphysis of long bones in children. Pain and swelling of the affected bone are characteristic features. X-rays show destruction and concentric layers of new bone formation.
- + A lumbar disc prolapse presents with pain in the lower back that can radiate into a buttock or down the leg. The white cell count and the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels would be normal in this condition.
- + Perthes' disease is osteochondritis of the epiphysis of the femoral head. Early X-rays show widening of the joint space. Later there is a decrease in the size of the nuclear femoral head with patchy density. The white cell count and ESR and CRP levels are unaffected.



A 30-year-old woman, being followed up for well-controlled systemic lupus erythematosus (SLE) and on low-dose steroids (prednisolone 5 mg/day), was noted to have an elevated creatinine by her GP. Investigations revealed: erythrocyte sedimentation rate (ESR) 20 mm in 1st hour; antibodies to double-stranded DNA (dsDNA) -ve, and antinuclear antibody (ANA) titre 1:80. Subsequent investigations, including a kidney biopsy, revealed World Health Organisation (WHO) class II disease (mesangial lupus nephritis).

Which one of the following would be the ideal treatment in this case?

A	No treatment needed
B	High-dose glucocorticoid pulses
C	High-dose glucocorticoid pulses + intravenous cyclophosphamide
D	High-dose glucocorticoid pulses + intravenous cyclophosphamide + azathioprine
E	Intravenous cyclophosphamide alone



A	No treatment needed
B	High-dose glucocorticoid pulses
C	High-dose glucocorticoid pulses + intravenous cyclophosphamide
D	High-dose glucocorticoid pulses + intravenous cyclophosphamide + azathioprine
E	Intravenous cyclophosphamide alone

## Explanation

### Treatment of SLE nephritis

Treatment of systemic lupus erythematosus (SLE) nephritis is based on the class of disease determined by renal biopsy and on disease activity.

World Health Organisation (WHO) disease classification:

I	Minimal change (normal on light microscopy)
II	Mesangial
III	Focal segmental proliferative
IV	Diffuse proliferative
V	Membranous
VI	Glomerulosclerosis

- + Patients with class I or class II disease have an excellent prognosis and usually do not require treatment.
- + Class III and class IV disease (proliferative nephritis) and class V nephritis are treated with high-dose steroids and adjunctive cyclophosphamide. Azathioprine and mycophenolate mofetil have also been found to be effective.
- + Class VI nephritis is advanced disease and is usually not treated.

A low erythrocyte sedimentation rate (ESR) and negative dsDNA (double-stranded DNA) antibodies indicate inactive disease.

A 26-year-old woman presents with a symmetrical small-joint polyarthritis, suspicious of rheumatoid arthritis, which has rapidly increased in severity over the last 3 months. She complains of morning stiffness on getting up for about the first hour of each morning and is having problems using her computer keyboard at her office.

On examination she has evidence of an active synovitis affecting her wrists and the small joints of her hands. She has limited movement of her elbows because of pain. Investigations show: haemoglobin 12.7 g/dl, white cell count  $8.3 \times 10^9/l$ , platelets  $212 \times 10^9/l$ , sodium 141 mmol/l, potassium 4.6 mmol/l, creatinine 95  $\mu\text{mol/l}$ . Rheumatoid factor is negative, anti-cyclic citrullinated peptide (anti-CCP) antibodies are positive.

Which one of the following factors is associated with the poorest prognosis?

- |   |                            |
|---|----------------------------|
| A | Young age                  |
| B | Male sex                   |
| C | Anti-CCP positivity        |
| D | Acute onset                |
| E | Negative rheumatoid factor |

A	Young age
B	Male sex
C	Anti-CCP positivity
D	Acute onset
E	Negative rheumatoid factor

## Explanation

### Prognostic factors in rheumatoid arthritis

Patients with rapid onset of rheumatoid arthritis appear to have a greater chance of remission, so the relatively acute onset seen here is not a poor prognostic indicator. Females tend to do worse than males with rheumatoid arthritis, and patients who acquire rheumatoid arthritis at a younger age appear to do better than older patients. With respect to antibodies directed against citrullinated peptide (anti-CCP antibodies), patients who are anti-CCP-positive, even those with rheumatoid factor negativity, do worse with respect to joint erosions and deformity.



A 62-year-old woman presents with severe pain and stiffness in her shoulder muscles and pelvis for the past 3 weeks that is worse in the mornings. Her erythrocyte sedimentation rate (ESR) is raised.

What is the most likely diagnosis?

A Polymyalgia rheumatica

B Polymyositis

C Pseudogout

D Psoriatic arthritis

E Rheumatoid arthritis

# Explanation

## Polymyalgia rheumatica

Stiffness, aching and pain in the muscles of the neck, shoulders, back, hips and thighs characterise the polymyalgia rheumatica syndrome. It is a form of giant-cell arteritis. The diagnosis is made from the history and symptoms. The erythrocyte sedimentation rate (ESR) is almost always remarkably high ( $> 40$  mm in 1st hour).

### Differential diagnosis

- + Symmetrical proximal muscle weakness resulting from muscle inflammation is seen in polymyositis, but pain is usually not a feature.
- + Pseudogout is the deposition of calcium pyrophosphate crystals in a joint that is already affected by arthritis. This is a non-inflammatory reaction so the erythrocyte sedimentation rate is not raised.
- + Psoriatic arthritis occurs in 20% of people with psoriasis. It affects mainly the distal interphalangeal joints.
- + Rheumatoid arthritis commonly affects the small joints of the wrist, hands and feet. Shoulder and pelvic involvement is rare and muscle weakness and tenderness is not seen.

In a population of 20 000 how many people would have rheumatoid arthritis in the western world?

A 1400

B 1000

C 200

D 100

E 50

A	1400
B	1000
C	200
D	100
E	50

## Explanation

### Prevalence of rheumatoid arthritis

The prevalence of rheumatoid arthritis has been consistently assessed as being between 0.8% and 1.1% of the adult population in cross-sectional studies in the United States and Western Europe, and translates into a higher prevalence in the elderly female population. Lower rates of 0.2–0.3% have been reported in China and Japan.



A 40-year-old man is being evaluated for recurrent mild haemoptysis. He gives a history of recurrent sinusitis. Blood investigations show: haemoglobin 12.8 g/dl; white cell count  $8.9 \times 10^9/l$ , erythrocyte sedimentation rate (ESR) 68 mm in 1st hour, urea 10 mmol/l, creatinine 180  $\mu\text{mol/l}$  and active sediments in the urine. The cytoplasmic antineutrophil cytoplasmic antibody (cANCA) is positive and the chest X-ray shows multiple cavities in both lung fields.

Which of the following statements is correct regarding his condition?

- |   |   |
|---|---|
| A | Upper respiratory tract biopsy is likely to show vasculitic changes |
| B | Granulomas are always seen in a renal biopsy                        |
| C | Lung biopsy has a high diagnostic yield                             |
| D | c-ANCA is highly specific in active disease, but is not sensitive   |
| E | c-ANCA is a useful marker for monitoring disease relapse            |

- |   |   |
|---|---|
| A | Upper respiratory tract biopsy is likely to show vasculitic changes |
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| E | c-ANCA is a useful marker for monitoring disease relapse            |

## Explanation

### Wegener's granulomatosis

Wegener's granulomatosis is a clinicopathological entity characterised by a triad of involvement of the upper respiratory tract, lower respiratory tract and kidneys, and is associated with a raised cytoplasmic antineutrophil cytoplasmic antibody (cANCA) serology. In active Wegener's disease with renal involvement, cANCA is highly sensitive and specific. However, after disease remission, it may remain elevated for years and is not useful in evaluating patients for relapse.

### Pathological findings

Biopsies of the:

- + upper respiratory tract show granulomas but not vasculitis
- + lung show granulomas and vasculitis
- + kidney show vasculitis and glomerulonephritis and occasional granulomata formation, although it is glomerulonephritis which is the dominant feature

A 40-year-old woman attends the Rheumatology Clinic complaining of marked intermittent pain in her right hand. Physical examination reveals a loss of pinprick sensation in the hand, mainly affecting the thumb and index finger. There is tingling and numbness involving the thumb, index and middle fingers.

Given the likely clinical diagnosis, which of the following clinical features is most likely to be noted with this condition?

- |   |   |
|---|---|
| A | Tingling and pain in the medial half of the palm            |
| B | Pain aggravated if the wrist is hyperextended for 2 minutes |
| C | Pain relieved by repetitive actions of the hand             |
| D | Pain occurring mainly during the day                        |
| E | Pain in the forearm and hand mainly at night                |



- |   |   |
|---|---|
| A | Tingling and pain in the medial half of the palm            |
| B | Pain aggravated if the wrist is hyperextended for 2 minutes |
| C | Pain relieved by repetitive actions of the hand             |
| D | Pain occurring mainly during the day                        |
| E | Pain in the forearm and hand mainly at night                |

## Explanation

### Carpal tunnel syndrome

Tingling and pain in the medial half of the palm is typical of ulnar neuritis, this option is therefore false. Pain due to carpal tunnel syndrome is especially common at night and after repetitive actions. Pain commonly involves not only the wrist and hand but also the forearms, along the distribution of the median nerve (rarely extending even further up the arm to the shoulder). Phalen's test consists of holding the wrist hyperflexed for 1-2 minutes, which reproduces the symptoms.



A 54-year-old woman complains of severe right shoulder pain that is localised mainly to the mid-humerus but also if felt diffusely around the anterolateral shoulder. The onset was sudden and not precipitated by trauma. Physical examination reveals limited abduction, with point tenderness over the subacromial bursa and the greater tuberosity of the humerus. A radiograph reveals a linear calcific density in the supraspinatus tendon.

Which one of the following statements fits best with the underlying condition?

- |   |   |
|---|---|
| A | The calcific density is most likely calcium urate crystals          |
| B | The calcific density is most likely calcium hydroxyapatite crystals |
| C | Trauma is the commonest cause of calcific tendonitis                |
| D | Commonest age of presentation is below 40 years                     |
| E | Physiotherapy is of no value in managing the condition              |

- |   |   |
|---|---|
| A | The calcific density is most likely calcium urate crystals          |
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| E | Physiotherapy is of no value in managing the condition              |

## Explanation

### Calcific tendinitis

The clinical features and radiographic pattern are characteristic of calcific tendinitis, an extremely common rheumatic syndrome characterised by deposits of hydroxyapatite crystals within injured rotator cuff muscles near the humeral attachment region. It most commonly involves the supraspinatus tendon, but the infraspinatus and subscapularis tendons may also be involved.

Patients usually respond to therapy with non-steroidal anti-inflammatory agents and physiotherapy might be useful. The tendinitis normally improves over the course of 4–6 weeks.

A 20-year-old man presents with a raised red and scaly lesion on his glans penis, red discoloration and pain in both eyes, and pain and swelling of his right knee. Over the past few days he has noticed painless red plaques on his hands and feet. A diagnosis of reactive arthritis is suspected.

Which clinical feature best supports a diagnosis of reactive arthritis?

A	History of a flu-like illness 4-6 weeks prior to symptoms
B	Presence of keratoderma blenorrhagica
C	Family history of ulcerative colitis
D	Positive gonococcal culture of urethral discharge
E	Arthritis affecting the upper limb joints

- |   |   |
|---|---|
| A | History of a flu-like illness 4-6 weeks prior to symptoms |
| B | <b>Presence of keratoderma blenorrhagica</b>              |
| C | Family history of ulcerative colitis                      |
| D | Positive gonococcal culture of urethral discharge         |
| E | Arthritis affecting the upper limb joints                 |

## Explanation

### Reactive arthritis

Reiter syndrome (now more commonly called reactive arthritis) is a triad of urethritis, arthritis and conjunctivitis, which follows 4-6 weeks after a genitourinary (chlamydial) infection. 'Reactive arthritis' is the term given to arthritis following gastrointestinal (shigella, Yersinia) infection. Keratoderma blenorrhagica (brown aseptic abscesses on the soles and palms) may occur. Ulcerative colitis may give rise to enteropathic arthritis. A urethral discharge in Reiter syndrome is usually sterile. The arthritis commonly affects the knees, ankles or feet.



An 11-year-old boy weighing 70 kg presents with limitation of abduction and internal rotation of the hip. There is tenderness in Scarpa's triangle on examination. On flexing the hip, external rotation of the limb occurs.

What is the most likely diagnosis?

- |   |                                 |
|---|---------------------------------|
| A | Perthe's disease                |
| B | Slipped upper femoral epiphysis |
| C | Transient synovitis of the hip  |
| D | Tuberculosis of the hip         |
| E | Juvenile spondyloarthropathy    |

A

Perthe's disease

B

Slipped upper femoral epiphysis

C

Transient synovitis of the hip

D

Tuberculosis of the hip

E

Juvenile spondyloarthropathy

Explanation

# Explanation

## The painful hip in a child

- + Slipped upper femoral epiphysis, the correct answer here, is displacement of the proximal femoral epiphysis. The direction of slip is always posterior and often medial. The change in range of hip motion is usually diagnostic.
- + Perthes' disease is osteochondritis of the head of the femur, which can be related to avascular necrosis of the hip. It occurs mainly in children aged 4-10 years and usually presents with a painless limp. On examination, the only striking sign is moderate limitation of all hip movements, with pain and spasm if movement is forced.
- + Transient synovitis of the hip is a benign, non-traumatic, self-limiting disorder that mimics septic arthritis. The cause is unclear, but it can be associated with immune responses to viral and bacterial antigens at the synovial membrane. The hip is usually held in flexion, abduction and external rotation. The joint is very painful and resistant to movement.
- + Tuberculosis of the hip is rarely seen in the UK. Young adults are usually affected. The joint is swollen and red. The pain is mild. There may be a sinus discharging pus or a palpable abscess. Movements of the hip are not impaired.
- + Juvenile spondyloarthropathy affects teenage and younger boys, mainly producing an asymmetric arthritis of lower-limb joints and enthesitis. It is associated with HLA B27 and an increased risk of acute anterior uveitis.

A 60-year-old patient has been complaining of a 1-month history of generalised headache, malaise and fever. He has also noticed scalp sensitivity while brushing his hair.

What is the most likely diagnosis?

A Transient ischaemic attacks

B Migraine

C Giant-cell arteritis

D Intracranial tumour

E Systemic sclerosis



# Explanation

## Giant-cell arteritis

The diagnosis of giant-cell arteritis depends on clinical suspicion in less typical cases. As with polymyalgia rheumatica, the onset can be dramatic and the condition always becomes fully developed over a period of only a few weeks, although the delay in diagnosis can be months.

### Clinical features

The malaise, fever and anaemia are similar to those in polymyalgia rheumatica; the differences are in the vascular symptoms. The majority of patients have temporal features, with headache, scalp sensitivity and tender, thickened arteries; the classic nodular, red streaks are unusual. Overwhelming generalised headache and the feared complication of irreversible loss of vision are more readily recognised.

The clinical features listed emphasise developing arteritis. A wide range of cranial manifestations reflects the involvement of larger arteries with an internal elastic lamina in the face, neck and brain base, but not in the cerebral vessels. They include headache, scalp tenderness, skin necrosis, jaw claudication while talking or chewing, tongue pain and claudication, and face and neck pain with nerve damage.

The visual manifestations, which include blurred vision, amaurosis fugax, transient and permanent blindness, diplopia and visual hallucinations, are caused by ischaemic changes in the ciliary arteries causing optic neuritis or infarction, with a smaller number of cases due to thrombosis of the central retinal artery.

A 7-year-old boy complains of having intermittent hip pain for several months. Haematological investigations are normal. X-rays show flattening of the femoral head.

What is the most probable diagnosis?

- |   |                                 |
|---|---------------------------------|
| A | Pyogenic arthritis              |
| B | Slipped upper femoral epiphysis |
| C | Fractured femur                 |
| D | Osteogenesis imperfecta         |
| E | Perthe's disease                |

D	Osteogenesis imperfecta
E	Perthe's disease

## Explanation

### Hip pain in a child

Perthes' disease is osteochondritis of the femoral head, and it affects children between 3 and 11 years of age. It presents with pain in the hip or knee and causes a limp. On examination, all movements at the hip are limited. Early X-rays show widening of the joint space. Later there is decrease in the size of the nuclear femoral head with patchy density. Later still there may be collapse and deformity of the femoral head with new bone formation. The white cell count, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels are unaffected.

A painful, hot, swollen joint with increased synovial fluid, indicated by the widened joint space on X-ray, is characteristic of pyogenic arthritis. The white cell count, ESR and CRP levels will be high in this condition.

Slipped upper femoral epiphysis affects children aged 10-16 years. Some 20% are bilateral. About half the patients are obese and hypogonadal. On examination flexion, adduction and medial rotation are limited. The upper femoral epiphysis is displaced from its normal position on the femoral neck. Displacement is always downwards and backwards so that the epiphysis comes to lie at the back of the femoral neck.

Osteogenesis imperfecta is an autosomal dominant disorder that results in brittle, fragile bones that fracture easily. X-rays reveal many fractures and translucent bones. There is no history of trauma or radiographic evidence in this case to suggest a fracture of the femur.



A 5-year-old girl presents with a 10-week history of pain in both knees and redness and pain in both eyes. Rheumatoid factor is negative but antinuclear antibody tests are positive.

What is the most probable diagnosis?

- |   |   |
|---|---|
| A | Extended oligoarthritis                     |
| B | Polyarticular juvenile idiopathic arthritis |
| C | Systemic arthritis                          |
| D | Persistent oligoarthritis                   |
| E | Enthesitis-related arthritis                |



# Explanation

## Persistent oligoarthritis

Persistent oligoarthritis is the most common form of juvenile idiopathic arthritis (50–60%). Four or fewer joints are affected, especially the knees, ankles and wrists. Girls, with a peak age incidence of 3 years, are most commonly affected. Uveitis is common in children with positive antinuclear antibodies.

## Differential diagnosis

- + Extended oligoarthritis is usually antinuclear antibody- and rheumatoid factor-negative.
- + Polyarticular juvenile idiopathic arthritis affects older girls (> 8 years of age). Arthritis commonly involves the small joints of the hands, wrists, ankles and feet.
- + Enthesitis-related arthritis (juvenile spondyloarthropathy) usually affects teenage boys, causing asymmetric arthritis of the lower-limb joints and associated with acute anterior uveitis.
- + Features of systemic arthritis (Still's disease), such as a fever, lymphadenopathy and hepatosplenomegaly are not seen in this case.

A 56-year-old woman presents with polyarthralgia and painful restricted movement of her fingers, Raynaud's syndrome, diarrhoea, weight loss of 6 kg and a facial rash. Her investigations reveal: normochromic normocytic anaemia, positive anticentromere (ANA) pattern, anti-dsDNA-negative). An anti-SM, ribonucleoprotein (RNP), Ro and La antibodies are negative.

What is the most likely diagnosis?

- |   |                                 |
|---|---------------------------------|
| A | CREST (limited scleroderma)     |
| B | Mixed connective tissue disease |
| C | Progressive systemic sclerosis  |
| D | Rheumatoid arthritis            |
| E | Systemic lupus erythematosus    |

## Explanation

### CREST syndrome

Anticentromere antibodies are very specific for CREST syndrome (calcinosis cutis, Raynaud's syndrome, oesophageal dysmotility, sclerodactyly and telangiectasia). Her facial rash is due to telangiectasia; her painful fingers are caused by a combination of Raynaud's and sclerodactyly. The diarrhoea and weight loss are secondary to sclerodermatous involvement of the bowel, with bacterial overgrowth and subsequent malabsorption.

Around 15–20% of patients with progressive systemic sclerosis are anticentromere-positive but are more commonly anti-scl 70-positive.

You are called to see a 14-year-old boy who has had a fever of unknown origin for the last 7 days. He also complains of redness of both eyes, redness and dryness of his lips and neck swelling. He had a rash on his trunk that disappeared 2 days ago. On examination, he has cervical lymphadenopathy and his palms and soles are red and oedematous.

Given the suspected diagnosis, what would be the most appropriate therapy?

- |   |   |
|---|---|
| A | Intravenous steroids                    |
| B | Topical steroids                        |
| C | Aspirin and intravenous immunoglobulins |
| D | Protease inhibitors                     |
| E | Erythromycin                            |



- |   |   |
|---|---|
| A | Intravenous steroids                    |
| B | Topical steroids                        |
| C | Aspirin and intravenous immunoglobulins |
| D | Protease inhibitors                     |
| E | Erythromycin                            |

## Explanation

### Management of Kawasaki disease

Combination therapy with intravenous immunoglobulin (IVIG) and aspirin during the acute phase of Kawasaki disease produces a more marked anti-inflammatory effect and reduction in coronary artery abnormalities than does aspirin alone. It is recommended that patients with acute disease are treated with a single 2 g/kg infusion of IVIG and aspirin (30–50 mg/kg per day) within the first 10 days from onset, and that the aspirin dose is reduced to 3–5 mg/kg per day, given as a single daily dose, after the temperature has normalised. This is because early use of immunoglobulins is thought to lead to a reduction in formation of coronary artery aneurysms versus use of aspirin alone.

Aspirin is discontinued if no coronary abnormalities have been detected on an echocardiogram by 6–8 weeks after the onset of illness, but is continued if there are coronary artery abnormalities.

A 65-year-old white male, who is a chronic smoker, presents with low back and hip pain. His serum alkaline phosphatase level is 1000 IU/l, calcium 2.25 mmol/l and phosphate 1.2 mmol/l. Other liver function tests are normal. He also complains of difficulty in hearing.

What is the probable diagnosis?

- |   |                                     |
|---|-------------------------------------|
| A | Squamous-cell carcinoma of the lung |
| B | Multiple myeloma                    |
| C | Osteomalacia                        |
| D | Osteoporosis                        |
| E | Paget's disease of bone             |

## Explanation

### Paget's disease of bone

This man has Paget's disease of bone, which commonly occurs after the age of 40 years. The classic presentation is with bone pain, bone deformity, deafness and pathological fractures. The diagnosis is established by the finding of a raised serum alkaline phosphatase level but normal liver function tests.

Both squamous-cell carcinoma of the lung and multiple myeloma are associated with hypercalcaemia caused by lytic lesions of bone. The serum biochemistry is usually normal in osteoarthritis, and in osteoporosis, which would not be associated with deafness.

A 20-year-old man complains he has had pain in his abdomen, knee and elbow for the last 7 days. He had an upper respiratory tract infection 4 weeks ago. He also has a rash on his buttocks and lower limbs.

What is the diagnosis?

A Henoch-Schönlein purpura

B Enteropathic arthritis

C Reactive arthritis

D Viral arthritis

E Sarcoidosis



A	Henoch-Schönlein purpura
B	Enteropathic arthritis
C	Reactive arthritis
D	Viral arthritis
E	Sarcoidosis

## Explanation

### Henoch-Schönlein purpura

Enteropathic arthritis is associated with ulcerative colitis and Crohn's disease. Henoch-Schönlein purpura is characterised by abdominal pain and arthritis, and may follow an upper respiratory tract infection. Non-thrombocytopenic purpura occurs over the buttocks and legs. Intussusception, rectal bleeding and renal involvement can also occur.

A 22-year-old man complains of having low back pain for the past 3 months. He has also noticed a swelling of his right second toe and has pain in his heels when he walks. He was treated for red eyes 6 months earlier.

Which investigation would be most likely to provide a clue as to the cause of his condition?

A Joint aspirate and microscopy for uric acid crystals

B Test for serum rheumatoid factor

C HLA testing

D X-ray of the foot

E X-ray of the sacroiliac joints

- |   |  |
|---|--|
| A | Joint aspirate and microscopy for uric acid crystals |
| B | Test for serum rheumatoid factor                     |
| C | HLA testing  |
| D | X-ray of the foot                                    |
| E | X-ray of the sacroiliac joints                       |

## Explanation

### Ankylosing spondylitis

This patient has ankylosing spondylitis (AS). The main lesion is spinal ankylosis with sacroiliac joint involvement. X-ray of the sacroiliac joints may show squaring of the vertebrae, erosions of the apophyseal joints and obliteration of the sacroiliac joints. Uveitis is common and may occur in 25% of patients with AS. Human leucocyte antigen (HLA) testing is rarely of value because of the high frequency of HLA B27 in the population.

Gout commonly presents in the first metatarsophalangeal joint as a painful, red, hot lesion. It does not cause conjunctivitis or uveitis. An X-ray of the foot would not provide a clue as to the diagnosis as the features are not typical of rheumatoid arthritis or osteoarthritis.

A 43-year-old woman presents with a 3-year history of progressive rheumatoid arthritis that has been partially responsive to various non-steroidal anti-inflammatory drugs (NSAIDs) and to low-dose oral corticosteroids. After the examination, you decide to treat her active arthritis with methotrexate, currently the most widely used and effective agent for rheumatoid arthritis.

Which one of the following features is typical of methotrexate therapy?

- |   |  |
|---|--|
| A | Clinical improvements are usually seen within the first week of therapy initiation |
| B | Bone marrow suppression is not seen with low-dose methotrexate therapy             |
| C | Yearly full blood count and liver function test monitoring is necessary            |
| D | Birth control measures must be in use before methotrexate is started               |
| E | Hepatic fibrosis is common in relation to prolonged use of the drug                |



- |   |  |
|---|--|
| A | Clinical improvements are usually seen within the first week of therapy initiation |
| B | Bone marrow suppression is not seen with low-dose methotrexate therapy             |
| C | Yearly full blood count and liver function test monitoring is necessary            |
| D | <b>Birth control measures must be in use before methotrexate is started</b>        |
| E | Hepatic fibrosis is common in relation to prolonged use of the drug                |

## Explanation

# Explanation

## Methotrexate therapy

Methotrexate is currently the best drug used to treat rheumatoid arthritis, with initial improvement seen in 3-6 weeks and peak efficacy in 4-6 months. Methotrexate is taken orally (7.5-15 mg/week) and tolerance may be increased by spacing the oral doses over 1-2 days, giving a single intramuscular injection each week and daily folic acid (1 mg/day) supplementation.

Laboratory tests such as full blood count (FBC), platelet count, alkaline phosphatase and AST are done every 4-6 weeks.

### Adverse effects

Adverse effects such as nausea, abdominal pain and diarrhoea are often seen, but serious toxicity is rare. Transient or sustained (1.5-2 times normal values) elevations in alkaline phosphatase and SGOT are commonly seen and, in the majority of patients, generally do not portend the development of hepatic fibrosis. The most toxic drug-related side-effects are pancytopenia, neutropenia, thrombocytopenia, pneumonitis and cirrhosis - all these are reasons to stop the medication.

Methotrexate is known to be teratogenic and should not be given to women with childbearing potential unless they are using an adequate method of birth control. Because of its potential effect on sperm, men should discontinue methotrexate 3-4 months before attempting conception.

A 57-year-old obese woman presents with numbness, tingling and burning on the anterolateral aspect of the thigh. On examination there is dysaesthesia (increased sensitivity to light touch) in the affected area. An X-ray of the hip joint is normal.

What is the most likely possible cause of her symptoms?

- |   |  |
|---|--|
| A | Meralgia paraesthetica                 |
| B | Trochanteric bursitis                  |
| C | Fracture of the femoral neck           |
| D | Avascular necrosis of the femoral head |
| E | Polymyalgia rheumatica                 |

A	Meralgia paraesthetica
B	Trochanteric bursitis
C	Fracture of the femoral neck
D	Avascular necrosis of the femoral head
E	Polymyalgia rheumatica

## Explanation

### Hip pain

- + This patient has meralgia paraesthetica. It is caused by entrapment of the lateral cutaneous nerve of the thigh beneath the inguinal ligament. Most patients are obese; weight reduction helps to relieve symptoms.
- + Trochanteric bursitis occurs as a result of trauma or unaccustomed exercise in most cases. The pain over the trochanter is worse on going up the stairs and when abducting the hip.
- + Fracture of the femoral neck usually occurs after a fall. There is pain in the groin and thigh, weight bearing is painful or impossible, and the leg is shortened and externally rotated. X-rays are diagnostic.
- + Avascular necrosis of the femoral head causes severe hip pain. Again the X-ray might show a well-demarcated area of increased bone density or collapse of the affected bone. Usually there would be an associated risk factor such as corticosteroid or heparin treatment.
- + Polymyalgia rheumatica causes a sudden onset of severe pain and stiffness of the shoulders, hips and lumbar spine. These symptoms are worse in the morning, lasting from 30 minutes to several hours. Systemic features of tiredness, fever, weight loss, depression and night sweats can also occur.



A 45-year-old woman complains of feeling tired, she also notices she has dysphagia, a dry mouth, a gritty sensation in her eyes and increased photosensitivity.

Which would be the most definitive test for the suspected diagnosis?

- |   |                           |
|---|---------------------------|
| A | Serum iron level          |
| B | Oesophagogastrosocopy     |
| C | Labial gland biopsy       |
| D | Schirmer's test           |
| E | Antineutrophil antibodies |

- |   |                           |
|---|---------------------------|
| A | Serum iron level          |
| B | Oesophagogastrosocopy     |
| C | Labial gland biopsy       |
| D | Schirmer's test           |
| E | Antineutrophil antibodies |

## Explanation

### Diagnosis of Sjögren syndrome

Biopsy and histology of the labial glands from behind the lower lip provides the most definitive diagnostic test of Sjögren syndrome. The area is anaesthetised with lidocaine containing adrenaline, and an incision 1.5 cm long allows access to five to ten glands (2–4 mm in diameter) that are removed by simple blunt dissection. A diagnosis of Sjögren syndrome depends on finding foci of periductular infiltrates of at least 50 lymphocytes and/or plasma cells at a density of more than one focus per 4 mm<sup>2</sup>.

A 54-year-old man with a history of obesity, type 2 diabetes and hypertension presents to the clinic complaining of pain in his right first metatarsophalangeal joint. He takes orlistat, ramipril, indapamide, amlodipine and metformin and has been taking over-the-counter ibuprofen for intermittent bouts of the same pain that have occurred over the past 18 months. On examination he has a blood pressure of 149/90 mmHg and a body mass index (BMI) of 31 kg.m<sup>2</sup>. He has pain, swelling and redness over the right first metatarsophalangeal joint. Investigations show: haemoglobin 13.1 g/dl, white cell count  $5.9 \times 10^9/l$ , platelets  $229 \times 10^9/l$ , sodium 141 mmol/l, potassium 4.4 mmol/l, creatinine 132  $\mu\text{mol/l}$ . X-rays show reduced joint space and calcification.

Which one of his drugs should be discontinued?

- |   |            |
|---|------------|
| A | Ramipril   |
| B | Amlodipine |
| C | Indapamide |
| D | Orlistat   |
| E | Metformin  |

- |   |            |
|---|------------|
| A | Ramipril   |
| B | Amlodipine |
| C | Indapamide |
| D | Orlistat   |
| E | Metformin  |

## Explanation

### Thiazide diuretics and gout

This man has gout, a condition associated with insulin resistance, obesity and type 2 diabetes. Indapamide as a member of the thiazide class is associated with raised serum uric acid, so discontinuing indapamide and substituting another antihypertensive is the management of choice. While metformin should be dose-reduced or discontinued when the creatinine rises above  $140 \mu\text{mol/l}$  or so in a male, in itself it is not associated with an increased risk of gout. His acute gout should be managed with a short course of non-steroidal anti-inflammatory drugs.



A 23-year-old woman comes to the Emergency Department a few days after returning from a holiday to Spain during which she admits to unprotected sex with two male partners. She is now suffering from dysuria and a purulent urethral discharge, and an acutely swollen, painful left knee. On examination she is pyrexial 38.1°C, pulse is 90/min and regular. You confirm a left knee effusion with severely limited flexion.

Investigations;

Hb	12.1 g/dl
WCC	$8.1 \times 10^9/l$
PLT	$203 \times 10^9/l$
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.5 mmol/l
Creatinine	90 micromol/l
ESR	80 mm/1 <sup>st</sup> hour
CRP	189 mg/l

Which of the following is the most important next step?

Which of the following is the most important next step?

A IV antibiotic therapy

B Knee X-ray

C Knee aspiration

D Oral corticosteroids

E Oral NSAIDS

## Explanation

The answer is Knee aspiration -

This patient may have oligoarthritis related to acute gonococcal infection. Confirming the diagnosis via knee aspiration is therefore the most appropriate next step. A high white count is needed to confirm septic arthritis, although gram negative diplococci may only be seen in 25%. Ceftriaxone IV is the drug of choice for gonococcal arthritis, repeat drainage and/or formal surgical drainage may also be required. Blind therapy without investigation is inappropriate, with oral corticosteroids having the potential to worsen joint damage.

A 46-year-old woman presents to the Rheumatology Clinic for review. She has a history of systemic lupus erythematosus (SLE). Currently she is maintained on 60 mg of prednisolone per day and you are considering introducing azathioprine as a second-line agent.

Her blood results show: haemoglobin 11.0 g/dl, white cell count  $7.1 \times 10^9/l$ , platelets  $130 \times 10^9/l$ , sodium 139 mmol/l, potassium 4.0 mmol/l, creatinine 130  $\mu\text{mol/l}$ , plasma viscosity 2.1 mPa/s (normal range 1.50–1.72 mPa/s).

The levels of which one of the following can be easily measured to assess the risk of azathioprine toxicity?

- |   |   |
|---|---|
| A | 6-mercaptopurine                        |
| B | Thiopurine S-methyltransferase activity |
| C | 6-thioguanine nucleotides               |
| D | Inosine triphosphatase activity         |
| E | 6-methylmercaptopurine                  |



- |   |   |
|---|---|
| A | 6-mercaptopurine                        |
| B | Thiopurine S-methyltransferase activity |
| C | 6-thioguanine nucleotides               |
| D | Inosine triphosphatase activity         |
| E | 6-methylmercaptopurine                  |

## Explanation

### Thiopurine S-methyltransferase (TPMT) assay

*TPMT* mutations lead to elevated levels of 6-mercaptopurine. 6-Mercaptopurine is associated with excessive bone marrow suppression. Over the past few years a TPMT assay has been developed which is available in most tertiary centres to assess potential risk: 6-mercaptopurine is the active metabolite of azathioprine, so that levels cannot be assessed until after azathioprine activity has actually started. The 6-thioguanine nucleotides are further downstream metabolites of 6-mercaptopurine.

A 72-year-old man with heart disease is on diuretics. He complains of stiff, painful hands and knees. On examination, Heberden's nodes are seen.

What is the most appropriate initial treatment?

- |   |                                     |
|---|-------------------------------------|
| A | Regular paracetamol                 |
| B | Allopurinol                         |
| C | Oral NSAIDs with gastric protection |
| D | Knee replacement                    |
| E | Joint aspiration and microscopy     |

A	Regular paracetamol
B	Allopurinol
C	Oral NSAIDs with gastric protection
D	Knee replacement
E	Joint aspiration and microscopy

## Explanation

### NSAIDs in the treatment of osteoarthritis

The presence of Heberden's nodes is characteristic of osteoarthritis. These nodes are seen in the distal interphalangeal joints. Oral non-steroidal anti-inflammatory drugs (NSAIDs) do not offer an advantage over regular paracetamol, as such regular paracetamol is the best option here, especially give his heart disease and diuretic treatment, Joint aspiration and microscopy would be inconclusive and knee replacement in an elderly patient with heart disease would be a risky procedure.

A 50-year-old man is transferred to your hospital with a presumptive diagnosis of tuberculosis. His chest radiograph shows nodular cavitating lesions in both lung fields. His urinalysis shows 50 red blood cells per high-power field and proteinuria +++. He is scheduled for bronchoscopy with transbronchial lung biopsy in the morning. That evening he has a sudden deterioration consisting of massive haemoptysis and progressive renal failure.

The most appropriate therapeutic intervention at this point would be supportive management and which one of the following?

- |   |  |
|---|--|
| A | Corticosteroids iv                                 |
| B | Antituberculous medications                        |
| C | Cyclophosphamide iv 4 mg/kg                        |
| D | Oral cyclophosphamide 2 mg/kg                      |
| E | Corticosteroids iv and cyclophosphamide iv 4 mg/kg |



A	Corticosteroids iv
B	Antituberculous medications
C	Cyclophosphamide iv 4 mg/kg
D	Oral cyclophosphamide 2 mg/kg
E	Corticosteroids iv and cyclophosphamide iv 4 mg/kg

## Explanation

### Wegener's granulomatosis

The involvement of the lower respiratory tract as well as renal involvement suggests Wegener's granulomatosis in this man. Wegener's granulomatosis has an annual incidence of 0.5/100,000, with a mean age at onset of 40 years.

#### Clinical features

Manifestations include chronic sinusitis, otitis media, haemoptysis, glomerulonephritis, necrotising skin lesions, polyarthrits, uveitis and episcleritis. Biopsy (often of the nasopharynx) is the best way to achieve a diagnosis.

#### Treatment

Treatment of Wegener's granulomatosis with cyclophosphamide has resulted in marked improvement in outcome of this condition. Because of the severity and sudden deterioration in this case, intravenous corticosteroids and cyclophosphamide would be indicated here.

A 35-year-old woman is diagnosed with systemic lupus erythematosus.

What is the most common finding on blood testing that would be of help in supporting a conclusion that she had active disease?

A Anti double-stranded DNA

B Rheumatoid factor

C VDRL-positive

D Low complement levels

E Anticardiolipin antibody

- |   |                          |
|---|--------------------------|
| A | Anti double-stranded DNA |
| B | Rheumatoid factor        |
| C | VDRL-positive            |
| D | Low complement levels    |
| E | Anticardiolipin antibody |

## Explanation

### Serology in SLE

- + Complement levels fall in systemic lupus erythematosus (SLE) due to the formation of immune complexes. Whilst the result is not necessarily specific it would act as a confirmatory test for a positive clinical opinion. Low complement levels are a constant feature in the active phase of the disease.
- + Anti-dsDNA is almost exclusive to SLE but estimates of positivity in patients with SLE vary from 30-70%.
- + Some 40% of cases test positive for rheumatoid factor.
- + The false-positive rate for syphilis serology is around 10%.
- + Some women have anticardiolipin antibody (lupus anticoagulant) and are prone to recurrent abortions, thrombosis and thrombocytopenia.

A 70-year-old woman presents with pain and swelling in both knees. An X-ray shows a rim of calcification of the lateral meniscus in both knees.

What will be the characteristic finding in the joint aspirate?

- |   |                                  |
|---|----------------------------------|
| A | Neutrophils                      |
| B | Needle-shaped crystals           |
| C | White turbid fluid               |
| D | Positively birefringent crystals |
| E | No abnormality                   |



- |   |                                  |
|---|----------------------------------|
| A | Neutrophils                      |
| B | Needle-shaped crystals           |
| C | White turbid fluid               |
| D | Positively birefringent crystals |
| E | No abnormality                   |

## Explanation

### Pseudogout

This woman has pseudogout, which is caused by calcium pyrophosphate deposition and is associated with calcification of joint cartilage (chondrocalcinosis). The diagnosis is made by finding weakly positive birefringent calcium pyrophosphate crystals in the synovial fluid. Many neutrophils are also seen in the joint aspirate; hence, pseudogout is often misdiagnosed as septic arthritis. White turbid fluid is characteristic of acute gouty arthritis.

A 45-year-old woman comes to the Rheumatology Clinic complaining of skin thickening on her hands with subcutaneous calcinosis, and leathery skin elsewhere. She also feels that her fingers feel particularly cold and very painful when she goes out, to the extent that she has started to wear gloves even in the summer. She also suffers from reflux oesophagitis and was started on omeprazole a few months ago.

On examination, her blood pressure is 155/90 mmHg, she has sclerodactyly and calcification in her hands, and you notice multiple telangiectasia. Investigations show: haemoglobin 11.0 g/dl, white cell count  $8.2 \times 10^9/\text{l}$ , platelets  $142 \times 10^9/\text{l}$ , anticentromere antibodies positive, sodium 139 mmol/l, potassium 5.0 mmol/l, creatinine 162  $\mu\text{mol/l}$ .

Which one of the following is the most likely cause of mortality related to her underlying disease?

- |   |                       |
|---|-----------------------|
| A | Bronchial carcinoma   |
| B | Chronic renal failure |
| C | Pulmonary fibrosis    |
| D | GI bleeding           |
| E | Oesophageal carcinoma |

A	Bronchial carcinoma
B	Chronic renal failure
C	<b>Pulmonary fibrosis</b>
D	GI bleeding
E	Oesophageal carcinoma

## Explanation

### Mortality in scleroderma

- + Two causes of death are particularly prominent in systemic sclerosis, these are death due to progressive pulmonary fibrosis, and death due to renal failure
- + Although the mortality from renal failure was considerably higher than that for progressive lung disease, increased use of ACE inhibitors and better management of scleroderma renal crisis has reversed this in recent years
- + The rate of oesophageal carcinoma may be increased in patients with CREST (calcinosis cutis, Raynaud's phenomenon, oesophageal hypomotility, sclerodactyly and telangiectasia) due to an increase in gastro-oesophageal reflux disease
- + A rise in the incidence of bronchial carcinoma is also seen
- + Telangiectasia can be associated with increased risk of gastrointestinal bleeding

A 50-year-old shopkeeper has plaques on the extensor surfaces of her upper limbs. She complains of pain in her hands. On examination there is a telescoping deformity of both index fingers. The nails show pitting and horizontal ridging.

From what is she most probably suffering?

- |   |                              |
|---|------------------------------|
| A | Reactive arthritis           |
| B | Systemic lupus erythematosus |
| C | Rheumatoid arthritis         |
| D | Arthritis mutilans           |
| E | Gouty arthritis              |



# Explanation

## Arthritis mutilans

This patient has psoriatic arthropathy. Arthritis mutilans affects 5% of such patients, causing attrition of bone and cartilage and resulting in loss of the joint and marked instability. The encasing skin appears invaginated and telescoped. Traction can pull the finger back to its original length.

The occurrence of nail changes is also characteristic of psoriatic arthropathy (85%).

A 45-year-old woman with a history of flitting joint pains comes to the Rheumatology Clinic for review. She has suffered from dry eyes and has felt like she has not had enough spit in her mouth to enable her to chew her food. On examination her eyes look red and sore, you notice cracking and drying of her lips. You suspect Sjögren's.

Which of the following would be supportive of a Sjögren's diagnosis?

- |   |   |
|---|---|
| A | Biopsy revealing salivary gland atrophy |
| B | Positive anti-CCP antibody              |
| C | Positive anti-smooth muscle antibody    |
| D | Salivary stones on imaging              |
| E | Schirmer's test 4mm after 5 minutes     |

## Explanation

The answer is Schirmer's test 4mm after 5 minutes

Schirmer's test is designed to production of tears, where a bent piece of filter paper is placed in the corner of the eye. Moisture tracking up >15mm is considered a normal result, whereas less than 5mm is a definitive positive result (i.e. significant reduction in tear production).

Sjögren's is associated with postive rheumatoid factor antibodies, positive anti-nuclear antibodies, antibodies against alpha-fodrin and Ro/La autoantigens. Biopsy reveals inflammatory cell infiltration rather than atrophy. Salivary stones on gland imaging would suggest another cause for her dry mouth apart from Sjögren's.

A patient with type 1 diabetes mellitus has been complaining of a 3-month history of right shoulder pain. She describes this as a frozen shoulder, and says it hurts to move her shoulder at all.

What is the most likely diagnosis?

A Rheumatoid arthritis

B Osteoarthritis

C Adhesive capsulitis

D Pseudogout

E Calcific tendonitis



## Explanation

### Adhesive capsulitis in diabetes

Associated microvascular disease causes abnormal collagen repair in people with diabetes, and this predisposes to adhesive capsulitis. Occasionally, fibrous strands are seen traversing the joint space. Patients with diabetes often present with fibrosis elsewhere (eg Dupuytren's contracture). Trauma, the associated transient inflammatory state with granulation tissue, and eventual fibrous adhesions and thickening of the capsule may give rise to adhesive capsulitis.

A 72-year-old man comes to the Emergency Department. He is previously well with a history of mild hypertension, controlled with Ramipril. He is a non-smoker. Over the past 3 months he has suffered from increasing pain in his hips and shoulders, and most recently, over the past 3 weeks has suffered from pain in his jaw when he eats a large meal, and on one occasion transient visual loss affecting his right eye. On examination his BP is 160/95 mmHg, pulse is 70/min and regular. He has mild tenderness over his temporal artery on the right hand side. ESR is elevated at 82 mm/1<sup>st</sup> hour.

Which of the following is the optimal management?

- A Prescribe 40mg oral Prednisolone per day
- B Prescribe 60mg oral Prednisolone per day
- C Admit for IV Methylprednisolone
- D Arrange an outpatient temporal artery biopsy
- E Prescribe Aspirin and Clopidogrel in combination

## Explanation

The answer is Admit for IV Methylprednisolone

This man has temporal arteritis and is at imminent risk of an ischaemic event. As such he should be admitted for IV Methylprednisolone. Patients who have jaw claudication only could be managed with oral corticosteroids. Arranging an outpatient temporal biopsy without initiating corticosteroids is clearly substandard practice.

With respect to clinical scenarios, it is important to remember that 4% of patients with temporal arteritis do not have an elevated ESR. It is not therefore impossible that we would be presented in the exam with just this scenario in the presence of a normal ESR.

A 67-year-old woman presents with a 10-week history of pain affecting the cervical spine, both shoulders, lumbar spine and both hips. Early morning stiffness lasts until lunchtime and she feels markedly tired. She has a low-grade pyrexia of 37.4 °C, bilateral knee effusions and a right carpal tunnel syndrome.

Investigations reveal: normochromic normocytic anaemia with haemoglobin 10.1 g/dl, erythrocyte sedimentation rate (ESR) 81 mm in 1st hour, C-reactive protein (CRP) 27 mg/l, negative rheumatoid factor, serum immunoglobulins and protein electrophoresis show a polyclonal increase in gammaglobulins and elevated  $\alpha_1$ - and  $\alpha_2$ -globulins.

What is the most likely diagnosis?

- |   |                         |
|---|-------------------------|
| A | Paraneoplastic syndrome |
| B | Polymyalgia rheumatica  |
| C | Polymyositis            |
| D | Rheumatoid arthritis    |
| E | Temporal arteritis      |



# Explanation

## Polymyalgia rheumatica

Polymyalgia rheumatica (PMR) usually affects elderly white females (female to male ratio 2:1, average age at presentation 70 years). The arthritis is symmetrical and accompanied by an acute-phase response. Immune complexes may be detected in the serum in cases of PMR and also within the muscle. These are thought to play a role in pathogenesis but as yet their diagnostic significance remains uncertain. The polyclonal increase in globulins is a marker of inflammation associated with PMR. Early morning stiffness, particularly of the hip and shoulder girdle with associated fatigue can be pronounced and may last for up to 2-3 hours each morning.

Transient synovitis can occur in PMR and this is the most likely cause of the knee effusions here. Carpal tunnel may be associated in up to 15% of cases.

Treatment is with a tapering dose of prednisolone, with treatment monitoring by symptom and erythrocyte sedimentation (ESR) response. Steroid treatment is often required for up to 2 years. Prognosis is usually favourable and relapse is rare.

A 58-year-old woman complains of severe unilateral temporal headaches and jaw pain when eating. A provisional diagnosis of giant-cell arteritis is made.

Which one of the following is a characteristic clinical feature of this condition?

- |   |  |
|---|--|
| A | All peripheral arteries are involved                       |
| B | It does not occur in the absence of polymyalgia rheumatica |
| C | Negative temporal artery biopsy excludes the disorder      |
| D | Treatment is monitored by measuring ESR levels             |
| E | NSAID treatment is an effective first line of management   |

- |   |  |
|---|--|
| C | Negative temporal artery biopsy excludes the disorder    |
| D | Treatment is monitored by measuring ESR levels           |
| E | NSAID treatment is an effective first line of management |

## Explanation

### Giant-cell arteritis

Giant-cell arteritis involves the cranial arteries. The superficial temporal artery is involved in most patients, providing a convenient biopsy site, but this is only the 'tip of the iceberg'. The topographic distribution of GCA, which reflects its predilection for the internal elastic lamina, includes the aortic arch and its branches. GCA does not cause a widespread intracranial cerebral vasculitis, because intracranial arteries lack an internal elastic lamina. GCA does involve cervicocephalic arteries, including the carotid and vertebral arteries.

### Investigation and treatment

Although a temporal artery biopsy from the affected side is the definitive diagnostic test, a negative biopsy does not exclude the condition as skip lesions may occur. Treatment is monitored using the erythrocyte sedimentation rate (ESR). Steroid treatment is obligatory as this significantly reduces the risk of irreversible visual loss and other focal ischaemic lesions. Non-steroidal anti-inflammatory drugs (NSAIDs) are less effective and should not be used.

### Presentation

An association with polymyalgia rheumatica is well known, with PMR being present in about 60% of cases of GCA. Neck, shoulder and pelvic girdle pain are common presenting symptoms, along with headache and scalp tenderness. Symptoms of claudication may also occur (e.g. jaw claudication, amaurosis fugax). Stroke and transient ischaemic attack may occur but not usually as a presenting complaint.



A 74-year-old man who had a dual-chamber permanent pacemaker inserted 5 days earlier presents with fever, back pain and diarrhoea. He has a past history of diverticulosis, hypertension and a myocardial infarction some 8 years earlier. On examination there is restricted movement due to back pain and localised tenderness over the lumbar spine. There are no neurological signs. He is pyrexial (37.8 °C). Investigations show: haemoglobin 13.8 g/dl, white cell count (WCC)  $13.9 \times 10^9/l$ , platelets  $201 \times 10^9/l$ , sodium 140 mmol/l, potassium 4.8 mmol/l, creatinine 110  $\mu\text{mol/l}$ , erythrocyte sedimentation rate (ESR) 85 mm in 1st hour.

Which one of the following is the most likely diagnosis?

- |   |                         |
|---|-------------------------|
| A | Prolapsed lumbar disc   |
| B | Staphylococcal discitis |
| C | Spinal epidural abscess |
| D | Pyelonephritis          |
| E | Ischaemic colitis       |



## Explanation

### Staphylococcal discitis

Given the proximity of his symptoms to the pacemaker insertion, the most likely diagnosis here is haematogenous spread of *Staphylococcus aureus*, introduced at the time of the procedure. Nuclear medicine scans and magnetic resonance imaging of the spine are the most sensitive ways of detecting changes consistent with discitis in the early stages of infection.

### Treatment

Parenteral therapy for a period of at least 6 weeks is recommended, with agents specifically targeting *Staphylococcus* infection. Cure is effected in the majority of patients, although up to 15% may suffer some form of permanent neurological deficit.

A 42-year-old woman with systemic lupus erythematosus (SLE) is treated with pulsed monthly intravenous cyclophosphamide for grade 4 nephropathy. She presents in the Emergency Department with a dry cough, shortness of breath and fever. Her last cyclophosphamide dose was 10 days ago.

Investigations reveal: white cell count (WCC)  $2.3 \times 10^9/l$  (lymphocyte count  $0.7 \times 10^9/l$ ), platelets  $81 \times 10^9/l$ , haemoglobin 10.5 g/dl, erythrocyte sedimentation rate (ESR) 56 in 1 hour, C-reactive protein (CRP) 43 mg/l. the blood gases show:  $PO_2$  7.2 kPa,  $Pco_2$  3.6 kPa (after walking up and down the department). A plain chest X-ray was unremarkable apart from some patchy pulmonary infiltration.

What is the likely diagnosis?

- |   |   |
|---|---|
| A | Pulmonary embolism                      |
| B | <i>Pneumocystis jirovecii</i> pneumonia |
| C | TB                                      |
| D | Pleuritis                               |
| E | Pericarditis                            |

- |   |   |
|---|---|
| A | Pulmonary embolism                      |
| B | <i>Pneumocystis jirovecii</i> pneumonia |
| C | TB                                      |
| D | Pleuritis                               |
| E | Pericarditis                            |

## Explanation

### Opportunistic infection in SLE

This patient is immunosuppressed and has pancytopenia. She has exercised-induced hypoxia. The most likely opportunist infection is *Pneumocystis jirovecii* pneumonia. It is less likely to be tuberculosis because her erythrocyte sedimentation rate (ESR) is relatively low and the chest X-ray appeared relatively normal.

A 45-year-old man presents with fever, malaise, weight loss and myalgia over the past month. You suspect polyarteritis nodosa and arrange to perform some blood tests.

Which abnormality would you be most likely to find?

A Elevated creatinine

B Anaemia

C Leucopenia

D Thrombocytosis

E Positive ANCA



A

Elevated creatinine

B

Anaemia

C

Leucopenia

D

Thrombocytosis

E

Positive ANCA

## Explanation

### Blood tests in polyarteritis nodosa

Anaemia of chronic disease is associated with polyarteritis nodosa (PAN). Leucocytosis is common and eosinophilia may be seen in 30% of cases. Thrombocytosis and/or anaemia may sometimes be present. PAN may occasionally be associated with hepatitis B antigenaemia. ANCA (antineutrophil cytoplasmic antibody) is only rarely positive in classic PAN. Raised creatinine is often present and is included in the list of diagnostic criteria from the American College of Rheumatology (1990):

Three of the following 10 criteria must be present to classify a vasculitis as PAN:

- + Weight loss of 4 kg or more
- + Livedo reticularis
- + Testicular pain/tenderness
- + Myalgia or leg weakness/tenderness
- + Mononeuropathy or polyneuropathy
- + Diastolic blood pressure greater than 90 mmHg
- + Elevated BUN and creatinine levels
- + Infection with hepatitis B virus (HBV)
- + Abnormality on arteriography

A 40-year-old man is admitted with severe bloody diarrhoea over the past 4 days associated with a swollen, painful right knee, swollen finger joints and red, raised lesions on both legs. He has had similar attacks in the past.

What is the most probable diagnosis?

A Enteropathic arthritis

B Whipple's disease

C Polyarteritis nodosa

D Felty's syndrome

E Reactive arthritis

# Explanation

## Enteropathic arthritis

This patient has enteropathic arthritis. It is an acute inflammatory oligoarthritis that occurs in 20% of people with Crohn's disease and in 12% of those with ulcerative colitis. The arthritis coincides with exacerbations of the underlying bowel disease, sometimes in association with aphthous mouth ulcers, iritis and erythema nodosum.

Whipple's disease is associated with diarrhoea, weight loss, arthralgia and the presence of Periodic acid-Schiff- (PAS-) positive macrophages within intestinal biopsies.



A 24-year-old man presents with a 5-month history of low back pain, radiating to his buttocks, and back stiffness that is worse in the morning and worse after periods of inactivity. There is also a history of diarrhoea.

Which one of the following signs is the most likely to be present?

- |   |                                 |
|---|---------------------------------|
| A | Exaggerated lumbar lordosis     |
| B | Positive femoral stretch test   |
| C | Positive Trendelenburg test     |
| D | Restricted straight-leg raising |
| E | Sacroiliac joint tenderness     |

- |   |                                 |
|---|---------------------------------|
| A | Exaggerated lumbar lordosis     |
| B | Positive femoral stretch test   |
| C | Positive Trendelenburg test     |
| D | Restricted straight-leg raising |
| E | Sacroiliac joint tenderness     |

## Explanation

### Sacroiliitis

These symptoms suggest sacroiliitis, inflammation of the sacroiliac joints, which can be an early pointer to the development of ankylosing spondylitis or can occur as part of a wider picture of seronegative arthritis. Patients are usually HLA B27-positive, and the condition is more common in men. The history of diarrhoea also raises the possibility of inflammatory bowel disease. Sacroiliitis or spondylitis is seen in around 5% of sufferers of inflammatory bowel disease.

### Treatment

Non-steroidal anti-inflammatory drugs (NSAIDs) may be useful for pain and, where there is proved inflammatory bowel disease, many patients are started on sulfasalazine, as this may be a useful disease-modifying agent for both bowel and joint disease.

Femoral stretch test is considered a screening test for nerve root compression, as is straight leg raise. Trendelenburg's test is used to determine lower limb venous valve competency.

A 65-year-old woman presents with severe pain and stiffness of her shoulders and neck that is worse in the mornings and lasts for more than an hour. Physical examination is unremarkable. Blood tests show a mild normocytic normochromic anaemia. Her erythrocyte sedimentation rate (ESR) is 77 mm in 1st hour.

What is the most likely diagnosis?

A Polymyalgia rheumatica

B Polymyositis

C Hypocalcaemia

D Painful arc syndrome

E Frozen shoulder

## Explanation

### Polymyalgia rheumatica

Polymyalgia rheumatica is common in older women and presents as aching and morning stiffness in the proximal muscles. A raised erythrocyte sedimentation rate (ESR) and/or C-reactive protein (CRP) level is a hallmark of this condition.

### Differential diagnosis of shoulder pain

- + Symmetrical proximal muscle weakness resulting from muscle inflammation is seen in polymyositis. There is wasting of the shoulder and pelvic girdle muscles with weakness. Pain and tenderness are uncommon features.
- + Painful arc syndrome can be caused by supraspinatus tendinitis, subacromial bursitis or calcification of the rotator cuff. This is usually unilateral.
- + In frozen shoulder, there is marked reduction of passive and active movement. Abduction to even 90° is impossible.

Hypocalcaemia presents with tetany, depression, carpopedal spasm and neuromuscular excitability (Chvostek's sign).



A 49-year-old man has pain on resisted abduction of the arm from 0-90°. Which tendon is affected to give this particular restriction of movement?

- A    Infrapinatus tendonitis
- B    Supraspinatus tendonitis
- C    Subscapularis tendonitis
- D    Teres minor tendonitis
- E    Bicipital tendonitis

A	Infraspinatus tendonitis
B	Supraspinatus tendonitis
C	Subscapularis tendonitis
D	Teres minor tendonitis
E	Bicipital tendonitis

## Explanation

### Painful and restricted shoulder movements

- + Pain in the 0-90° range of movement is due to supraspinatus tendinitis.
- + Pain from 90-180° is due to involvement of the acromioclavicular joint.
- + Pain on internal and external rotation of the shoulder is due to involvement of the subscapularis and infraspinatus tendons.
- + Inflammation of the biceps tendon results in pain on resisted supination and flexion of the forearm.

A 10-year-old girl presents with a high fever, rash, and hip and knee joint pains. A slit-lamp examination of her eyes is normal. Blood tests are negative for autoantibodies, her eosinophil count is in the normal range and urine is negative for blood and protein.

What is the most likely diagnosis?

- |   |                              |
|---|------------------------------|
| A | Persistent oligoarthritis    |
| B | Still's disease              |
| C | Polyarticular arthritis      |
| D | Enthesitis-related arthritis |
| E | Henoch-Schönlein purpura     |

# Explanation

## Still's disease

This girl has Still's disease (juvenile systemic arthritis). It accounts for 10% of all cases of juvenile idiopathic arthritis and is seen more often in prepubertal girls with mono- or polyarticular synovitis, often preceded by fevers, an evanescent pink maculopapular rash, pericarditis, pneumonitis, lymphadenopathy and hepatosplenomegaly. Autoantibodies are negative.

## Differential diagnosis of juvenile arthritis

- + Persistent oligoarthritis is the most common form of juvenile idiopathic arthritis (JIA) (50-60%). It affects mainly very young girls who are about 3 years old. Uveitis (often with a positive antinuclear antibody) occurs in this condition.
- + Polyarticular juvenile idiopathic arthritis is rheumatoid factor-positive. Initially the arthritis commonly involves the small joints of the hands, wrists, ankles and feet. The rheumatoid factor-negative form is more common and usually affects girls under 12 years of age. They might be antinuclear antibody- (ANA-) positive, with a risk of chronic uveitis. The arthritis is often asymmetric, with a distribution similar to that seen in rheumatoid factor-positive cases.
- + Enthesitis-related arthritis affects teenage and younger boys, mainly producing an asymmetric arthritis of lower limb joints and enthesitis. It is associated with HLA B27 and a risk of acute anterior uveitis.
- + Henoch-Schönlein purpura is the commonest systemic vasculitis seen in children. It often occurs after upper respiratory tract infections. Lower limb purpura, polyarthrititis and abdominal pain occur. Haematuria and proteinuria due to glomerulonephritis are seen in 50% of cases.



A 23-year-old man presents with pain in both buttocks, and redness and mild pain in his right eye.

Given the most likely clinical diagnosis, which of the following clinical signs would be the earliest evidence of this condition?

- |   |  |
|---|--|
| A | Paraspinal muscle wasting                          |
| B | Retention of lumbar lordosis during spinal flexion |
| C | Reduction in chest expansion                       |
| D | Fixed flexion deformity of the hip                 |
| E | Visual field defects                               |

- |   |  |
|---|--|
| A | Paraspinal muscle wasting                          |
| B | Retention of lumbar lordosis during spinal flexion |
| C | Reduction in chest expansion                       |
| D | Fixed flexion deformity of the hip                 |
| E | Visual field defects                               |

## Explanation

### Ankylosing spondylitis

Retention of lumbar lordosis during spinal flexion is an early sign of ankylosing spondylitis. Paraspinal muscle wasting develops later. Costochondritis occurs in some patients, causing anterior chest pain and a measurable reduction in chest expansion. Acute anterior uveitis presents with severe eye pain, photophobia and blurred vision. Visual field defects do not occur. Hip joint involvement is usually a late occurrence.

A 21-year-old man presents with episodic pain in his buttocks, low back pain and stiffness that is worst in the mornings. A lateral X-ray of his lower spine shows blurring of the upper and lower vertebral rims at the thoracolumbar junction. He is found to be HLA B27-positive.

Given his likely diagnosis, what would be the most appropriate treatment?

A	Aspirin
B	Prednisolone
C	Diclofenac
D	Physiotherapy
E	Dextropropoxyphene

A	Aspirin
B	Prednisolone
C	Diclofenac
D	Physiotherapy
E	Dextropropoxyphene

## Explanation

### Early management of ankylosing spondylitis

This patient has ankylosing spondylitis. The key to the effective management of this condition is early diagnosis, so that a regimen of preventive exercises may be started before syndesmophytes have formed. The exercises aim to maintain spinal mobility, posture and chest expansion. Pain relief is an adjunct to physiotherapy. Steroid therapy is unhelpful.



A 44-year-old man presents with a sudden onset of pain, swelling and redness of his left big toe. He has no past medical history of note, and takes no regular medication. On examination his BP is 145/85 mmHg, pulse is 80/min and regular. His BMI is 32. Blood tests show: urea 5.6 mmol/l (normal range 2.5–7.5 mmol/l), creatinine 107  $\mu$ mol/l (60–110  $\mu$ mol/l) and urate 625  $\mu$ mol/l (230–460  $\mu$ mol/l).

What would be the drug of choice in this case?

A	Naproxen
B	Colchicine
C	Prednisolone
D	Allopurinol
E	Probenecid

A

Naproxen

B

Colchicine

C

Prednisolone

D

Allopurinol

E

Probenecid

## Explanation

### Treatment of acute gout

High urate levels are suggestive of acute gout. Non-steroidal anti-inflammatory drugs (NSAIDs) are usually the first-line treatment. The use of NSAIDs in high doses rapidly reduces the pain and swelling.

- + In individuals with renal impairment or with a history of peptic ulcer, alternative treatments can be considered, which include colchicine and intramuscular or intra-articular depot methylprednisolone, although prednisolone should also be used with care in renal impairment
- + While colchicine is a well proven medication for gout, it is not the preferred medication for the treatment of acute gout when there is no significant past medical history. It is most effective during the first 12-24 hours of an attack, but its effectiveness declines with the duration of inflammation. Moreover, when used to treat an acute attack, colchicine causes adverse GI effects, particularly diarrhoea and vomiting, in 80% of patients. As such in this patient, with no GI or cardiac history, naproxen is preferred
- + Allopurinol is indicated only under cover of a course of an NSAID or colchicine, and never within a month of an acute attack
- + Uricosuric agents (probenecid) are used in individuals who are allergic to allopurinol or they may be given with allopurinol in cases of severe tophaceous gout with high urate levels

A 45-year-old woman presents to the Emergency Department with monoarthritis affecting her right knee. She has a past history of mild asthma, which is managed with a Salbutamol inhaler, but nil else of note. Over the past few months she has been gaining a little weight. Uric acid is normal and x-rays of the knee reveal calcification consistent with pseudogout. Her BP is 145/82 mmHg, and pulse is 72/min and regular. Her BMI is 26.

Which of the following investigations is most likely to reveal the underlying cause?

A Thyroid function tests

B Fasting glucose

C Serum copper

D Serum ferritin

E Serum PTH



## Explanation

The answer is Thyroid function testing

Hypothyroidism, Wilson's disease, haemochromatosis and hyperparathyroidism are all diseases with a recognised association to pseudogout. The clue here is the gradual weight gain, which is a pointer to hypothyroidism as the underlying cause, and the fact that the other options such as Wilson's and haemochromatosis are substantially rarer than thyroid disease.

Whilst serum ferritin is elevated in haemochromatosis, it is transferrin saturation that is the gold standard investigation for diagnosing the condition. Wilson's usually presents at a younger age, either with an asymptomatic elevation in transaminases, psychiatric disturbance, ataxia or signs of chronic liver disease.

A 54-year-old woman has been experiencing increased pain and stiffness in her hands, wrists, upper arms, shoulders and calves for 2 years. She describes transient swelling at the wrists. She is frequently roused from sleep by pain and complains of marked fatigue with little stiffness sometimes associated with tingling in the hands, arms and feet. Review of systems reveals increasing urinary urgency and recurrent attacks of headaches.

On examination there is no significant abnormality apart from multiple tender spots over the spine and limbs, corresponding to bony prominences and to muscular tissue. Blood tests reveal a white blood cell count (WCC) of  $4 \times 10^9/l$  and a platelet count of  $167 \times 10^9/l$ . The erythrocyte sedimentation rate is 20 mm in 1st hour. The rheumatoid factor is negative and the antinuclear antibody (ANA) test comes back positive at 1:40. The creatine kinase and thyroid function tests are within normal limits.

Which one of the following is the most probable diagnosis?

- |   |                              |
|---|------------------------------|
| A | Systemic lupus erythematosus |
| B | Fibromyalgia syndrome        |
| C | Chronic fatigue syndrome     |
| D | Hypothyroidism               |
| E | Depression                   |



# Explanation

## Fibromyalgia syndrome

Fibromyalgia syndrome (FMS) is a common syndrome that is characterised by diffuse persistent musculoskeletal pain, stiffness, tenderness, sleep disturbance and easy fatigability. It typically affects women predominantly between the ages of 30 and 60 years. The American College of Rheumatology (ACR) 1990 criteria for the classification of FMS allows positive identification of the syndrome, which include:

- + A history of widespread pain which has been present for at least 3 months.
- + Pain on digital palpation in at least 11 of the following 18 tender-point sites (each of which is bilateral): occiput, low cervical, trapezius, supraspinatus, second rib, lateral epicondyle, gluteal, greater trochanter, knee.

On physical examination, patients with primary FMS usually appear well with no obvious systemic illness or articular abnormalities. Tenderness is the feature that most readily allows separation of FMS from other disorders that produce widespread pain or fatigue (as in chronic fatigue syndrome).

Laboratory and radiological investigations in FMS are largely unrevealing and primarily useful in searching for the presence of concomitant disorders. Even among normal blood donors the incidence of a positive antinuclear antibody (ANA) is approximately 5% when the screening is done with a serum dilution of 1:40. The titre of the ANA test is usually over 1:160 in the systemic connective tissue diseases.

Differential diagnosis: Certain rheumatic and non-rheumatic diseases can also mimic FMS, with similar symptoms (mostly pain and fatigue) and must be considered and treated even when the FMS has been positively identified; examples include depression and hypothyroidism.

A 50-year-old man is referred with a 2-week history of fever, arthralgia and weight loss. During his hospital stay he develops epigastric pain and notices difficulty dorsiflexing his left great toe. His blood pressure is 160/95 mmHg. Laboratory studies reveal: haemoglobin 10 g/dl, mean corpuscular volume (MCV) 98 fl, erythrocyte sedimentation rate (ESR) 100 mm in 1st hour and polymorphonuclear leucocytosis. The chest X-ray is clear.

Which of the following is the most likely diagnosis?

- |   |                              |
|---|------------------------------|
| A | Wegener's granulomatosis     |
| B | Systemic lupus erythematosus |
| C | Polyarteritis nodosa         |
| D | Polymyalgia rheumatica       |
| E | Churg-Strauss syndrome       |



# Explanation

## Polyarteritis nodosa

This patient presents with generalised features, abdominal pain, hypertension and mononeuritis. The raised erythrocyte sedimentation rate (ESR) and polymorphonuclear leucocytosis support a diagnosis of vasculitis, in this case polyarteritis nodosa. The abdominal pain is highly suggestive of mesenteric ischaemia. Mononeuritis multiplex develops because of involvement of the vasa vasorum; it is reflected in the patient's describing sudden loss of ability to dorsiflex his left great toe.

## Differential diagnosis

Wegener's granulomatosis and Churg-Strauss syndrome are commonly associated with pulmonary manifestations, which are absent in this case, and the chest X-ray is normal. Systemic lupus erythematosus (SLE) is more common in young women. Polymyalgia rheumatica presents with pain and stiffness in the shoulder and pelvic girdles, but hypertension and mononeuritis are not recognised features of the disorder.

A 30-year-old man who is being managed by the ophthalmologists for anterior uveitis is referred to you for an opinion. He is now suffering from painful genital ulcers and a rash which resembles erythema nodosum. On examination he has oral aphthous ulcers and ulcers on his scrotum. Other history of note includes diarrhoea, which his GP thought was due to irritable bowel syndrome. Investigations show: haemoglobin 11.9 g/dl, white cell count  $8.1 \times 10^9/l$ , platelets  $231 \times 10^9/l$ , C-reactive protein (CRP) 65 mg/l (normal range is  $< 10$  mg/l), sodium 139 mmol/l, potassium 4.5 mmol/l, creatinine 110  $\mu$ mol/l.

Which one of the following is the most likely diagnosis?

A	Behcet's disease
B	SLE
C	Wegener's granulomatosis
D	Polyarteritis nodosa
E	Ulcerative colitis

## Explanation

### Behçet's disease

This presentation is highly suggestive of Behçet's disease. Laboratory findings are non-specific and are those of acute inflammation, with raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). While autoantibody studies may prove positive in some patients, they do not confirm the presence of Behçet's disease. Neurological and renal manifestations of Behçet's disease may also occur, particularly in patients with more prolonged disease. Mortality is up to 16% at 5 years, with thrombosis, neurological involvement or pulmonary/coronary artery aneurysm rupture being common modes of death.

A 61-year-old woman who has suffered from rheumatoid arthritis for 30 years comes to the Neurology Clinic for review. She has been suffering extreme pain at the back of her neck radiating to her occiput. Apparently the pain also radiates down both arms, and she has lost fine motor control of her hands, finding it difficult to partake in her hobby of needlework. The pain is intermittent and some days are very much worse than others. Examination reveals increased tone in both upper limbs, with 4/5 power weakness and hyper-reflexia. She has extensive evidence of joint damage related to rheumatoid arthritis.

Which of the following is the most likely diagnosis?

- |   |                          |
|---|--------------------------|
| A | Atlantoaxial subluxation |
| B | Cervical spondylosis     |
| C | Syringobulbia            |
| D | Syringomyelia            |
| E | Cervical disc prolapse   |



## Explanation

The answer is Atlantoaxial subluxation

The intermittent nature of the symptoms and the long history of rheumatoid arthritis raises the possibility of atlantoaxial subluxation. Occult instability can be identified on a lateral cervical spine view, an atlantoaxial distance of  $>4\text{-}5\text{mm}$  is indicative of instability, and flexion, neutral and extension views are recommended. Once symptoms of spinal cord compression occur, surgical fusion is the only recommended option.

Cervical spondylosis symptoms are often seen after an episode of trauma, as are symptoms associated with cervical disc prolapse, and are unlikely to be intermittent as is seen here. A prominent feature of syrinx formation is sensory loss in a cape distribution over the shoulders, which does not fit with the clinical description.

A 27-year-old woman presents to the Rheumatology Clinic. She complains of arthritis affecting her knees, elbows, wrists, ankles and the small joints of her fingers. She has also had fever and weight loss of 4 kg over the past 5 months. On examination, she has hepatomegaly and arthritis over a joint distribution that is consistent with rheumatoid arthritis.

Which one of the following investigations would be most indicative of a diagnosis of adult-onset Still's disease?

- |   |                                |
|---|--------------------------------|
| A | Positive rheumatoid factor     |
| B | Positive anti-nuclear antibody |
| C | Raised ESR                     |
| D | Raised ferritin                |
| E | Positive anti-CCP antibodies   |

- |   |                                |
|---|--------------------------------|
| A | Positive rheumatoid factor     |
| B | Positive anti-nuclear antibody |
| C | Raised ESR                     |
| D | Raised ferritin                |
| E | Positive anti-CCP antibodies   |

## Explanation

### Diagnosis of adult Still's disease

Raised antinuclear antibody, rheumatoid factor and raised erythrocyte sedimentation rate are all well-known findings in patients with established rheumatoid arthritis. Markedly raised ferritin is, however, more specifically associated with Still's disease. Rheumatoid factor is also found less commonly in patients with Stills, (<10%). Anti-cyclic citrullinated peptide (anti-CCP) antibodies are found more commonly in patients with rheumatoid arthritis than those with adult-onset Still's disease.

A 49-year-old woman visits her GP complaining that her fingers become white/blue and painful when she goes out into the cold. Past medical history of note includes prescription of an asthma inhaler by her GP for symptoms of increased shortness of breath, and reflux for which she takes intermittent omeprazole. She also has joint pains which she self-medicates with ibuprofen tablets.

On examination she is hypertensive at 145/92 mmHg and has telangiectasia. You notice soft-tissue calcification and sclerodactyly on examination of her hands. Investigations show: haemoglobin 12.0 g/dl, white cell count  $5.4 \times 10^9/\text{l}$ , platelets  $180 \times 10^9/\text{l}$ , sodium 140 mmol/l, potassium 4.9 mmol/l, creatinine 140  $\mu\text{mol/l}$ .

Which one of the following antibodies is most likely to be found in this patient?

- |   |                    |
|---|--------------------|
| A | Anti-centromere    |
| B | Anti-smooth muscle |
| C | Anti-GBM           |
| D | Rheumatoid factor  |
| E | P-ANCA             |



A	Anti-centromere
B	Anti-smooth muscle
C	Anti-GBM
D	Rheumatoid factor
E	P-ANCA

## Explanation

### CREST syndrome

This patient has the features of CREST syndrome (calcinosis cutis, Raynaud's phenomenon, oesophageal dysmotility, sclerodactyly and telangiectasia). This is associated with anticentromere antibodies in about 90% of cases. Calcinosis is usually easily identified on plain radiographs, and oesophageal dysmotility is seen on barium swallow.

### Management

The goal of pharmacotherapy is to reduce morbidity and to prevent complications where possible, Raynaud's is typically managed with calcium antagonists, proton-pump inhibitors are used for symptoms of reflux, and prostaglandins, PDE-5 inhibitors and endothelin-receptor antagonists are used to manage associated pulmonary hypertension.

A 35-year-old ship's steward is started on a new drug for rheumatoid arthritis before leaving for Africa. He returns after 4 months complaining of hair loss and blurring of vision. It is found that he has misread the prescription and is taking double the prescribed dose daily.

Which drug is most likely to cause these symptoms?

- |   |                    |
|---|--------------------|
| A | Gold               |
| B | D-Penicillamine    |
| C | Hydroxychloroquine |
| D | Diclofenac         |
| E | Sulfasalazine      |

# Explanation

## Side-effects of treatments for rheumatoid arthritis

- + Hydroxychloroquine may decrease visual acuity and, albeit rarely, cause retinopathy. Visual monitoring (6-12-monthly) is essential for all patients prescribed hydroxychloroquine.
- + Gold is given by deep intramuscular injection weekly, with close monitoring of the full blood count and urinalysis for protein prior to each injection. It would not be an appropriate medication for this patient.
- + D-Penicillamine and sulfasalazine may cause pancytopenia and also need close monitoring. They do not, however, cause hair loss and blurring of vision.

A 67-year-old man presents with a 2-year history of pain and stiffness in both knees. You suspect osteoarthritis.

Which one of the following clinical findings would be most important in deciding how best to manage his condition?

- |   |  |
|---|--|
| A | Severity of pain and stiffness in the knees                    |
| B | Crepitus elicited on movement of the joints                    |
| C | Presence of subchondral sclerosis in radiographs               |
| D | Fissuring and surface erosion of cartilage seen on arthroscopy |
| E | Fixed-flexion deformity  |



A	Severity of pain and stiffness in the knees
B	Crepitus elicited on movement of the joints
C	Presence of subchondral sclerosis in radiographs
D	Fissuring and surface erosion of cartilage seen on arthroscopy
E	Fixed-flexion deformity

## Explanation

### Management of osteoarthritis

The guiding principle in the management of osteoarthritis is to treat the symptoms and disability, not the clinical or radiological appearances. Educating the individual about the disease and its effects reduces pain, distress and disability and increases compliance with treatment. Psychological or social factors alter the impact of the disease.

A 56-year-old woman with known severe rheumatoid despite therapy with Etanercept and Methotrexate comes to the clinic for review. She has been feeling increasingly tired over the past few months and her GP has found her to be neutropaenic (neutrophil count  $1.1 \times 10^9/l$ ) on routine blood testing. In the clinic she looks a little pale and tired. There are signs of active joint disease affecting her fingers and wrists. Abdominal examination reveals evidence of splenomegaly.

What other abnormality would you expect on investigation?

- |   |   |
|---|---|
| A | Anti dsDNA antibodies                             |
| B | Hepatic fibrosis                                  |
| C | Myeloid hypoplasia on bone marrow examination     |
| D | Positive ANCA                                     |
| E | Restrictive pattern on pulmonary function testing |

## Explanation

The answer is Positive ANCA -

The triad of active joint disease, neutropaenia and splenomegaly raises the possibility of underlying Felty's syndrome. The neutropaenia is thus unlikely to be linked to prescription of Methotrexate. Positive ANCA specifically to lactoferrin is found in approximately 2/3rds of cases of Felty's, whereas anti dsDNA antibodies are only occasionally seen. Myeloid hyperplasia, with premature arrest of cell development is normally seen in the bone marrow, rather than myeloid hypoplasia. Anti-nuclear antibodies and anti-glucose 6 phosphate isomerase antibodies are also seen in significant numbers of patients with Felty's. One differential for Felty's is the large granular lymphocyte (LGL) syndrome, where a clonal population of abnormal lymphocytes is seen.

A 49-year-old man with a history of psoriasis presents to the Rheumatology Clinic with a deforming small joint polyarthritis particularly affecting the DIP joints of the fingers, and to a lesser extent his wrists and elbows. He has active skin disease, for which his GP has prescribed topical corticosteroids. He is unable to continue his job as an electrician due to pain in his hands. On examination there is nail pitting and obvious psoriasis affecting the backs of his elbows, his knees and his scalp.

Investigations;

Hb	12.0 g/dl
WCC	$10.1 \times 10^9/l$
PLT	$189 \times 10^9/l$
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	90 micromol/l
ESR	65 mm/1 <sup>st</sup> hour
Glucose	4.9 mmol/l

Which of the following is the most appropriate next intervention?



Which of the following is the most appropriate next intervention?

- A Ibuprofen
- B Infliximab
- C Methotrexate
- D Naproxen
- E Oral corticosteroids

## Explanation

The answer is Methotrexate -

In this situation, with active skin disease and arthritis, a traditional DMARD that will act positively on both aspects is the most appropriate next step. Weekly Methotrexate is therefore the correct answer. Psoriasis responds well to anti-TNF therapies; in the event that the response to Methotrexate is inadequate, an anti-TNF agent is an appropriate next step. NSAIDs can be added for relief of symptoms. Leflunomide and Sulphasalazine are alternative traditional DMARDs to Methotrexate.

A 47-year-old woman presents with an inability to raise her arms over her shoulders. Over the past few weeks she has also been having difficulty swallowing food. On examination there is muscle wasting and the muscles are tender, with reduced tendon reflexes. Her serum creatine kinase is elevated.

What is the most likely diagnosis?

A Polymyalgia rheumatica

B Polymyositis

C Hypocalcaemia

D Painful arc syndrome

E Frozen shoulder

# Explanation

## Polymyositis

In polymyositis there is symmetrical proximal muscle weakness resulting from muscle inflammation. Dysphagia, dysphonia and respiratory weakness can develop. Diagnosis is by measurement of creatine kinase, electromyography (EMG) and muscle biopsy.

### Differential diagnosis

- + Polymyalgia rheumatica is common in older women and presents as aching and morning stiffness in the proximal muscles. There is very little or no muscle tenderness and reflexes are normal.
- + Painful arc syndrome can be due to supraspinatus tendinitis, subacromial bursitis or calcification of the rotator cuff. This is usually unilateral.
- + In frozen shoulder there is marked reduction of passive and active movement. Abduction even to  $90^\circ$  is impossible. Muscle wasting, tenderness and reduced tendon reflexes are not seen in this condition, however.

Hypocalcaemia presents with tetany, depression, carpopedal spasm and neuromuscular excitability (Chvostek's sign).



A 48-year-old man presents to the clinic complaining of painful hands and fingers. On examination he has bilateral sausage-shaped fingers and pain over the distal interphalangeal joints. His nails are also pitted. There is no other past medical history of note.

His blood results show: haemoglobin 14.0 g/dl, platelets  $180 \times 10^9/l$ , white cell count  $8.1 \times 10^9/l$ , C-reactive protein (CRP) 46 mg/l, rheumatoid factor negative, sodium 140 mmol/l, potassium 5.0 mmol/l, creatinine 100  $\mu\text{mol/l}$ .

Which one of the following is the most likely diagnosis?

A Rheumatoid arthritis

B Psoriatic arthritis

C Gout

D Osteoarthritis

E Post viral arthritis

## Explanation

### Psoriatic arthritis

The picture of symmetrical distal polyarthrititis, dactylitis and nail pitting is very typical of psoriatic arthritis. Nail pitting may be the only visible sign of psoriasis and frank skin plaques do not necessarily have to be present. Most patients are rheumatoid factor-negative, although case series report positive rheumatoid factor in 5–9% of patients.

### Treatment

Initial treatment is with non-steroidal anti-inflammatory drugs, although tumour necrosis factor alpha (TNF- $\alpha$ ) plays an integral role in the pathogenesis of the disease, and anti-TNF- $\alpha$  antibodies have joined a range of other second-line therapies like sulfasalazine, methotrexate and ciclosporin in the management of the condition.

A 74-year-old man is noted to have purplish-coloured right third and fourth toes 4 days after coronary angiography and a creatinine level of 240  $\mu\text{mol/l}$  (the creatinine level was normal on admission). He has a history of adult-onset diabetes mellitus, hypertension and a 50 pack-year smoking history. Cholesterol crystal atheromatous embolisation is suspected.

Which one of the following statements about cholesterol embolisation is true?

- A Anticoagulants reduce the risk of cholesterol embolisation
- B Diabetes mellitus is associated
- C Abnormal creatinine on admission does not increase risk
- D Thrombolysis is of proven benefit
- E Diuretics are the mainstay of treatment

- |   |  |
|---|--|
| A | Anticoagulants reduce the risk of cholesterol embolisation |
| B | Diabetes mellitus is associated                            |
| C | Abnormal creatinine on admission does not increase risk    |
| D | Thrombolysis is of proven benefit                          |
| E | Diuretics are the mainstay of treatment                    |

## Explanation

### Atheromatous embolisation

Cholesterol crystal (atheromatous) embolisation is a common occurrence in patients with advanced atherosclerotic disease but is often either not recognised or misdiagnosed as 'vasculitis'. The exact incidence is currently unknown, but it is associated with significant morbidity and mortality. With a rise in the number of geriatric patients with atherosclerosis, the recognition of this disorder is critical to prevent unnecessary diagnostic studies and treatment with high-dose corticosteroids/cytotoxic agents, which are of no benefit.

The source of most cholesterol emboli is the abdominal aorta, iliofemoral or renal arteries, but cardiac and thoracic aorta sources have been described. Diabetes mellitus and abnormal creatinine levels before an investigation increase the risk of developing the condition.



A 22-year-old girl presents for review. She has recently suffered a viral upper respiratory tract infection, diagnosed by her general practitioner (GP) as glandular fever. Progressive tiredness has followed and she presents to the Emergency Department for review. On further questioning she admits to haemoptysis but her GP put this down to the infection.

Urine examination reveals the presence of blood and protein, and an admission creatinine is  $342 \mu\text{mol/l}$ . She is admitted to the renal ward, and renal biopsy and staining reveals a linear pattern of immunoglobulin G (IgG) deposition against the glomerular basement membrane.

What diagnosis fits best with this clinical picture?

- |   |                          |
|---|--------------------------|
| A | Goodpasture's syndrome   |
| B | Henoch-Schönlein purpura |
| C | IgA nephropathy          |
| D | Membranous nephropathy   |
| E | Wegener's granulomatosis |

# Explanation

## Goodpasture syndrome

The microscopy and staining here reveals the presence of linear immunoglobulin G (IgG) deposition (anti-glomerular basement membrane or anti-GBM antibody). Goodpasture syndrome can present with asymptomatic proteinuria or microscopic haematuria, acute nephritic syndrome, nephrotic syndrome or chronic renal failure.

Management of Goodpasture syndrome involves the use of combination cytotoxic therapy and corticosteroids. Severe pulmonary haemorrhage responds to plasma exchange, which can be performed in a number of specialist immunology units.

Recurrent Goodpasture syndrome can occur in response to repeated viral infections.

A 40-year-old woman complains of pain and stiffness in the small joints of her hands, especially in the mornings. An X-ray shows only soft-tissue swelling, but magnetic resonance imaging reveals erosions at the metacarpophalangeal joints.

Which one of the following indicates a worse than average prognosis?

A	Anaemia occurring a year after onset
B	Negative IgM rheumatoid factor
C	Male patient
D	Positive IgG rheumatoid factor
E	Gradual onset over a few months

- |   |                                      |
|---|--------------------------------------|
| A | Anaemia occurring a year after onset |
| B | Negative IgM rheumatoid factor       |
| C | Male patient                         |
| D | Positive IgG rheumatoid factor       |
| E | Gradual onset over a few months      |

## Explanation

### Prognostic indicators in rheumatoid arthritis

This patient most probably has rheumatoid arthritis. A worse than average prognosis (with a predictive accuracy of 80%) is indicated by:

- + Female sex
- + Gradual onset over a few months
- + Positive IgM rheumatoid factor
- + Anaemia developing within 3 months of onset
- + Anti-CCP antibody positivity (associated with more aggressive joint disease)



A 64-year-old woman presents with a 3-month history of tiredness, fever, weight loss and pain and stiffness in her shoulders and neck. She has now developed a severe headache. Physical examination reveals tenderness over the temporal region. Blood tests show: haemoglobin 10.5 g/dl (normal range 11.5–16.5 g/l), erythrocyte sedimentation rate (ESR) 80 mm in 1st hour (normal range 0–30).

What is the most probable diagnosis?

- |   |                          |
|---|--------------------------|
| A | Polymyositis             |
| B | Temporal arteritis       |
| C | Neurosarcoidosis         |
| D | Chronic fatigue syndrome |
| E | Migraine                 |

- |   |                          |
|---|--------------------------|
| A | Polymyositis             |
| B | Temporal arteritis       |
| C | Neurosarcoidosis         |
| D | Chronic fatigue syndrome |
| E | Migraine                 |

## Explanation

### Giant-cell arteritis

This patient most probably has giant-cell arteritis, which is an inflammatory granulomatous arteritis of large arteries that occurs in association with polymyalgia rheumatica. It affects people over the age of 50 years. A raised erythrocyte sedimentation rate (ESR) is a hallmark of this condition. There can also be a mild normocytic normochromic anaemia.

In polymyositis, there is progressive proximal muscle weakness, with wasting of the shoulder and pelvic girdle muscles. Headache is not a feature of this disorder. Chronic fatigue syndrome occurs most commonly in women between the ages of 20 and 40 years. The cardinal symptom is generalised fatigue made worse by exertion. Mood disorders and sleep disturbances also occur. Migraine is a recurrent headache associated with visual and gastrointestinal disturbance. Tingling, numbness and weakness on one side can occur during an attack. The patient is usually asymptomatic between episodes of migraine attacks. There are no characteristic investigative findings and the diagnosis is usually clinical.

A 60-year-old patient has been complaining of a 1-month history of generalised headache, malaise and fever. He has also noticed scalp sensitivity while brushing his hair.

What is the definite test to confirm the suspected diagnosis?

A MRI scan

B CT scan

C ESR

D Temporal artery biopsy

E Antinuclear antibody test

A	MRI scan
B	CT scan
C	ESR
D	Temporal artery biopsy
E	Antinuclear antibody test

## Explanation

### Diagnosis of giant-cell arteritis

Temporal artery biopsy is the definitive diagnostic test for giant-cell arteritis. A 2-cm segment of a tender artery will provide positive histology in 70% of cases. The diagnostic rate may be enhanced by taking longer segments or by the biopsy of other tender scalp vessels. While biopsy confirmation of the diagnosis is important, it should not be a reason for withholding steroids because characteristic pathological features persist for at least 2 weeks after treatment has begun, and some argue that scar change never clears.



A 39-year-old woman complains of swelling, stiffness and pain in her fingers. She also tells her doctor that in winter her fingers often turn dark in colour. Her autoimmune screen shows the presence of anticentromere antibody.

Which one of the following is she most likely to have?

- |   |                              |
|---|------------------------------|
| A | Rheumatoid arthritis         |
| B | Systemic lupus erythematosus |
| C | Pseudogout                   |
| D | Polyarteritis nodosa         |
| E | CREST variant of scleroderma |

- |   |                              |
|---|------------------------------|
| A | Rheumatoid arthritis         |
| B | Systemic lupus erythematosus |
| C | Pseudogout                   |
| D | Polyarteritis nodosa         |
| E | CREST variant of scleroderma |

## Explanation

### Anticentromere antibodies

Antibodies to centromere are a subset of antinuclear antibodies, which most commonly occur in the CREST variant of scleroderma (CREST = calcinosis cutis, Raynaud's phenomenon, oesophageal hypomotility, sclerodactyly and telangiectasia).

They are uncommon in the diffuse form of scleroderma. They are rarely present in rheumatoid arthritis, systemic lupus erythematosus (SLE) or polyarteritis nodosa.

An elderly man, who had a left hip replacement 2 years ago, now presents with right hip pain. An X-ray of the affected area shows an increased trabecular pattern and cortical thickening of the right hemipelvis, with narrowing of the joint space and osteophyte formation. Routine blood tests are normal except for serum alkaline phosphatase, which is elevated to 477 IU/l.

What is the probable reason for his right hip pain?

- |   |                                    |
|---|------------------------------------|
| A | Osteoarthritis                     |
| B | Rheumatoid arthritis               |
| C | Osteoarthritis with cholelithiasis |
| D | Paget's disease of bone            |
| E | Osteosarcoma                       |

# Explanation

## Paget's disease of bone

The X-ray findings and elevated serum alkaline phosphatase with normal serum calcium and phosphate levels are characteristic of Paget's disease of bone. This may cause bony pain due to secondary osteoarthritis or pathological fractures. Osteosarcoma is a rare but serious complication of Paget's disease and presents as a sudden increase in pain and swelling of an affected bone.



An elderly man with recently diagnosed heart failure is being treated with diuretics. He now develops severe joint pain in his left ankle, with swelling and redness.

Which investigation would be the most important in making a diagnosis?

- |   |                                    |
|---|------------------------------------|
| A | X-ray ankle                        |
| B | Serum uric acid estimation         |
| C | Serum creatinine                   |
| D | Joint fluid microscopy and culture |
| E | ESR                                |

- |   |                                    |
|---|------------------------------------|
| A | X-ray ankle                        |
| B | Serum uric acid estimation         |
| C | Serum creatinine                   |
| D | Joint fluid microscopy and culture |
| E | ESR                                |

## Explanation

### Gout as a side-effect of diuretics

Gouty arthritis may be precipitated by diuretic therapy. Joint fluid microscopy would show the presence of long, needle-shaped uric acid crystals that are negatively birefringent under plane polarised light. Serum uric acid levels are not usually raised in acute gout. The joint fluid would be sterile. Erythrocyte sedimentation rate (ESR) estimation and X-ray of the ankle would not provide a diagnosis.

A 28-year-old man presents with pain in his left arm. Until recently he has worked as a chef but was forced to give up this work because he had difficulty sensing when objects were hot to touch and was frequently getting burned. On examination he has mild bilateral weakness of the biceps, triceps and finger muscles, with absent biceps, triceps and brachioradialis reflexes. There is reduced pinprick sensation over a diffuse area involving both upper limbs and the shoulder areas, but vibration and joint position sense are preserved. He has a mild increase in tone affecting both legs. Investigations show: haemoglobin 12.4 g/dl, white cell count  $5.9 \times 10^9/l$ , platelets  $231 \times 10^9/l$ , erythrocyte sedimentation rate (ESR) 12 mm in 1st hour, sodium 141 mmol/l, potassium 4.3 mmol/l, creatinine 110  $\mu\text{mol/l}$ , glucose 5.2 mmol/l.

Which one of the following is the most likely diagnosis?

- |   |                      |
|---|----------------------|
| A | Neuralgic amyotrophy |
| B | Cervical myelitis    |
| C | Meningioma           |
| D | Multiple sclerosis   |
| E | Syringomyelia        |

## Explanation

### Syringomyelia

The loss of pain and temperature sensation, but with preservation of joint position and vibration sense is a relatively typical of presentation with syringomyelia. Diffuse muscle atrophy begins in the hands and spreads proximally, eventually involving the shoulder girdle. Patients suffer increased tone in the lower limbs, which may eventually progress to a spastic paraparesis. Proximal extension of the syrinx may produce symptoms of syringobulbia. Magnetic resonance imaging is the diagnostic modality of choice to confirm the condition.



A 65-year-old woman with a 30-year history of rheumatoid arthritis presents with severe shoulder pain and pain during the middle portion of arm abduction. She says the pain came on suddenly whilst reaching for a heavy cooking pan. An X-ray of the shoulder is normal.

What is the most likely cause of her symptoms?

- A Rotator cuff tendonitis
- B Torn rotator cuff
- C Frozen shoulder
- D Calcific tendonitis
- E Polymyalgia rheumatica

## Explanation

### Torn rotator cuff in rheumatoid arthritis

A torn rotator cuff can occur spontaneously in elderly patients with rheumatoid arthritis. The patient is able to abduct the arm, but the pain worsens during the middle of the range of abduction.

### Differential diagnosis

- + Adhesive capsulitis (true frozen shoulder) is a rare condition in which there is severe shoulder pain and complete loss of all shoulder movements.
- + Calcific tendinitis is due to calcium pyrophosphate deposits in the tendon that would be apparent on X-ray. The condition is not always symptomatic.
- + Polymyalgia rheumatica causes a sudden onset of severe pain and stiffness of the shoulders and neck. These symptoms are worse in the morning and last from 30 minutes to several hours. Tiredness, fever, weight loss, depression and occasionally nocturnal sweats also occur in this condition.

Which of the following is a potentially fatal complication of microscopic polyangiitis, but not of classic PAN?

- A Renal failure
- B Bowel perforation
- C Myocardial infarction
- D Pulmonary haemorrhage
- E Cerebrovascular accident

- |   |                          |
|---|--------------------------|
| A | Renal failure            |
| B | Bowel perforation        |
| C | Myocardial infarction    |
| D | Pulmonary haemorrhage    |
| E | Cerebrovascular accident |

## Explanation

### Polyarteritis nodosa

Though described here first, classic polyarteritis nodosa (classic PAN), ie a necrotising vasculitis of small- and medium-sized muscular arteries, is felt to be less common than microscopic polyangiitis (microscopic polyarteritis), which affects capillaries, venules and arterioles.

#### Clinical features

- + Classic PAN does not involve pulmonary arterioles and death is usually the result of renal failure, gastrointestinal complications (infarct/perforation) and cardiovascular causes.
- + In contrast, death in patients with microscopic polyangiitis is usually the result of renal failure or pulmonary haemorrhage. Stroke and congestive heart failure due to intractable hypertension lead to additional late mortality and morbidity.



A 51-year-old woman presents to the clinic complaining of symptoms of knee pain and restricted movement, coupled with clicking. She has a history of hypertension currently managed with Ramipril but nil else of note. On examination her BP is 135/75 mmHg, pulse is 80/min and regular. Her BMI is 32. The left knee has restricted flexion and creptus on movement. There is wasting of the quadriceps. She is already taking regular paracetamol.

Which other step is she likely to benefit from most?

A Wedge insert in her shoes

B Arthroscopy and washout

C Regular NSAIDs

D Weight loss

E Gentle jogging

# Explanation

The answer is Weight loss

This woman is obese with a BMI of 32, and any offloading of weight is likely to substantially impact on pain related to her osteoarthritis. Exercise would help, but this should be supported resistance exercise rather than jogging which may further exaggerate her knee pain. Osteoarthritis has at best a minor inflammatory component, as such NSAIDs are not indicated. Wedge inserts were supported as a treatment for both medial and lateral compartment knee arthritis, but a recent study (JAMA 2013), does not support an impact on symptoms of pain. At this stage, arthroscopy and washout is not indicated at least until the benefits of weight loss are evaluated.

<http://jama.jamanetwork.com/article.aspx?articleid=1730513>

A 75-year-old woman complains of increasing pain and swelling in both ankles, with stiffness and decreased mobility. She also has painful finger joints with nodules at the proximal and distal interphalangeal joints. Over the past 2 weeks she has had increasing difficulty in passing urine and dysuria.

What is the most likely cause of her joint symptoms?

- |   |                      |
|---|----------------------|
| A | Reiter's syndrome    |
| B | Rheumatoid arthritis |
| C | Osteoporosis         |
| D | Osteoarthritis       |
| E | Behçet's disease     |

# Explanation

## Osteoarthritis

This is a case of osteoarthritis of the ankles and hands. The nodules at the proximal interphalangeal joints are called Bouchard's nodes and those at the distal interphalangeal joints are called Heberden's nodes.

The dysuria is unrelated to the osteoarthritis and could be due to urethral syndrome as a consequence of the menopause.



A 70-year-old man with a long history of cervical spondylosis presents with pain, tingling and numbness in both arms. He has increased tone, hyper-reflexia and upgoing plantars on examination of the lower limbs.

What would the most appropriate treatment be in his case?

- |   |                        |
|---|------------------------|
| A | Bedrest                |
| B | Analgesia and sedation |
| C | Neurosurgical referral |
| D | Soft support collar    |
| E | Cervical root block    |

- |   |                        |
|---|------------------------|
| A | Bedrest                |
| B | Analgesia and sedation |
| C | Neurosurgical referral |
| D | Soft support collar    |
| E | Cervical root block    |

## Explanation

### Cervical spondylosis

Bilateral root pain with paraesthesiae in patients with cervical spondylosis, accompanied by lower limb upper motor neurone signs, is a neurosurgical emergency because a central disc prolapse may compress the cervical spinal cord. Neurosurgical referral is therefore essential in this case.

In monosodium urate monohydrate arthropathy, what is the most characteristic feature seen on examination of the synovial fluid?

- A Orange colour of synovial fluid
- B Rhomboid shape of the crystals
- C Positive birefringence of the crystals when seen under polarised light
- D Presence of long needle-shaped crystals
- E Presence of crystals within lymphocytes

- |   |  |
|---|--|
| A | Orange colour of synovial fluid  |
| B | Rhomboid shape of the crystals   |
| C | Positive birefringence of the crystals when seen under polarised light |
| D | <b>Presence of long needle-shaped crystals</b>                         |
| E | Presence of crystals within lymphocytes                                |

## Explanation

### Synovial fluid in gout

A high concentration of monosodium urate monohydrate (MSUM) crystals in chronic gout can make the synovial fluid appear white.

Calcium pyrophosphate crystals are small and rhomboid in shape and are positively birefringent under polarised light. MSUM crystals are typically long and needle-shaped and show negative birefringence. In acute gout, the number of neutrophils is greatly increased in synovial fluid: these phagocytose the urate crystals.



A 66-year-old woman has sustained two vertebral fractures following minor trauma and is diagnosed with osteoporosis. Initially she is treated with bisphosphonate but the treatment is stopped because of side-effects. You are considering raloxifene as an alternative therapy.

In your advice to the patient you should inform her that this therapy can cause which one of the following?

- A Improve the bone mineral density in the spine and hips
- B Increase the risk of breast cancer
- C Cause vaginal bleeding at the end of each month of therapy
- D Increase the high density lipoprotein (HDL) levels
- E Increase the risk of clotting

D Increase the high density lipoprotein (HDL) levels

E Increase the risk of clotting

## Explanation

### Raloxifene

- + Activity: Raloxifene is a selective oestrogen-receptor modulator that exerts both oestrogen-agonist effects on bone and lipid metabolism and oestrogen-antagonist effects on uterine endometrium and breast tissue.
- + The most common adverse effects of raloxifene are hot flushes and leg cramps. The drug is also associated with an increased risk of thromboembolic events.
- + Beneficial effects: The beneficial oestrogenic activities of raloxifene include a lowering of total and low-density lipoprotein cholesterol levels and augmentation of bone mineral density. Raloxifene reduces fracture risk at the spine but not at the hip. In women with a previous vertebral fracture, the magnitude of this reduction has been found to be dose-dependent and at least four times greater in women with no previous fracture.
- + Raloxifene vs oestrogen: Raloxifene does not raise triglyceride or high-density lipoprotein (HDL) cholesterol levels. It does not have some of the troublesome side-effects of oestrogen, such as vaginal spotting (bleeding) or breast tenderness. Raloxifene might have fewer side-effects than are typically observed with oestrogen therapy because of its tissue selectivity.

A previously fit and well 24-year-old presents to the Emergency Department with a swollen and painful left calf. There is no past medical history. On examination she has mottled-looking legs bilaterally and a swollen left calf. Investigations reveal: white cell count (WCC)  $5.4 \times 10^9/\text{l}$  (lymphocytes  $1.5 \times 10^9/\text{l}$ , neutrophils  $3.3 \times 10^9/\text{l}$ ), platelets  $86 \times 10^9/\text{l}$ , activated partial thromboplastin time 55s, erythrocyte sedimentation rate (ESR) 18 mm in 1st hour and C-reactive protein (CRP) 2 mg/l.

What is the most likely diagnosis?

- |   |                                     |
|---|-------------------------------------|
| A | Primary antiphospholipid syndrome   |
| B | Secondary antiphospholipid syndrome |
| C | Homocystinuria                      |
| D | SLE                                 |
| E | Factor V Leiden deficiency          |



A	Primary antiphospholipid syndrome
B	Secondary antiphospholipid syndrome
C	Homocystinuria
D	SLE
E	Factor V Leiden deficiency

## Explanation

### Antiphospholipid syndrome

The phospholipid antibody syndrome is characterised by the triad of:

- + Thrombocytopenia
- + Recurrent thromboses
- + Recurrent miscarriage

Clinical features include the presence of livedo reticularis. It can either be primary (existing on its own) or secondary (usually associated with systemic lupus erythematosus or SLE). The absence of evidence for SLE - ie no raised erythrocyte sedimentation rate (ESR), lymphopenia or typical clinical history - suggests that this is primary disease in this case. This diagnosis is further supported by the paradoxically raised activated partial thromboplastin ratio.

### Management

Recurrent thrombosis in the presence of antiphospholipid syndrome is an indication for lifelong warfarin therapy. It should be noted that warfarin is teratogenic and if this woman ever plans to conceive she would have to be transferred to low-molecular-weight heparin injections.



A 75-year-old woman with a long history of rheumatoid arthritis complains of chest pain and breathlessness. On examination she has tachycardia. Her blood pressure is 80/60 mmHg and an electrocardiogram (ECG) shows low QRS voltages.

What is the most likely cause of her condition?

- A Aortic dissection
- B Constrictive pericarditis
- C Acute pericarditis
- D Cardiac tamponade
- E Hypertrophic cardiomyopathy

- |          |                             |
|----------|-----------------------------|
| A        | Aortic dissection           |
| B        | Constrictive pericarditis   |
| C        | Acute pericarditis          |
| <b>D</b> | <b>Cardiac tamponade</b>    |
| E        | Hypertrophic cardiomyopathy |

## Explanation

Pericardial effusion in rheumatoid arthritis

Pericardial effusions are more common in patients with rheumatoid arthritis than constrictive pericarditis and acute pericarditis. This woman has cardiac tamponade secondary to pericardial effusion caused by rheumatoid arthritis.

In acute pericarditis, the ECG is diagnostic. Initially there is ST-segment elevation in all leads facing the epicardial surface. Later on the ST segment normalises and T-wave inversion may be seen.

Hypertrophic cardiomyopathy is a familial autosomal dominant condition in the majority of cases. Young adults are most affected. The ECG shows left ventricular hypertrophy and ST and T-wave changes. Abnormal Q waves, most commonly in the inferolateral leads, occur in 25-50% of patients. There is no known association with rheumatoid arthritis.

A 19-year-old woman presents with a painful left hip and groin and is unable to weight-bear. She completed therapy for acute myeloblastic leukaemia some 6 months earlier. On examination, she walks with a limp and there is limitation of hip flexion, internal and external rotation. Investigations show: haemoglobin, 12.1 g/dl, white cell count  $6.1 \times 10^9/l$ , platelets  $191 \times 10^9/l$ , sodium 140 mmol/l, potassium 4.7 mmol/l, creatinine 130  $\mu\text{mol/l}$ , C-reactive protein (CRP) 12 mg/l. The left hip X-ray shows joint sclerosis with collapse of the femoral head.

Which one of the following is the most likely diagnosis?

- |   |                    |
|---|--------------------|
| A | Septic arthritis   |
| B | Gout               |
| C | Pseudogout         |
| D | Avascular necrosis |
| E | Osteoarthritis     |

A	Septic arthritis
B	Gout
C	Pseudogout
D	Avascular necrosis
E	Osteoarthritis

## Explanation

### Secondary avascular necrosis

Secondary avascular necrosis may occur as a result of corticosteroid use and malignancy, including chemotherapy. Two uncontrolled studies suggest that bisphosphonates can delay complete collapse of the femoral head, and statins given at the same time as corticosteroids may reduce the chances of developing avascular necrosis, although both of these studies were in an older population.

### Management

Transtrochanteric rotational osteotomy is the surgical intervention of choice, which works by moving the diseased section of the femoral head out of the weight-bearing line, moving weight-bearing to what was previously the posterior surface, although of course total hip replacement will eventually be required.



A 47-year-old woman complains of exertional dyspnoea associated with a dry cough and bloody discharge from her nose. Her ankles, fingers and toes are swollen. Blood tests for antibodies are positive for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA).

What is the most likely diagnosis?

- |   |  |
|---|--|
| A | Churg-Strauss syndrome                         |
| B | Systemic lupus erythematosus                   |
| C | Wegener's granulomatosis                       |
| D | Rheumatoid arthritis with fibrosing alveolitis |
| E | Goodpasture's syndrome                         |

## Explanation

### Wegener's granulomatosis

Wegener's granulomatosis is a small-vessel necrotising vasculitis and commonly presents with upper airway involvement (typically epistaxis, nasal crusting and sinusitis), haemoptysis, mucosal ulceration and deafness due to serous otitis media. Renal vasculitis may occur. The characteristic immune marker is the cytoplasmic (sometimes called 'classic') antineutrophil cytoplasmic antibody (cANCA). The principal antigen in the cytoplasm has now been identified as being proteinase 3.

A 40-year-old woman who is a keen gardener presents to her GP complaining of pain in her right elbow. She is right-handed and has spent the past 2 weeks planting bulbs in the garden.

Which one of the following features would be most suggestive of a diagnosis of tennis elbow?

A Pain on pressure over the medial epicondyle

B Pain on wrist flexion against resistance

C Pain on wrist pronation

D Pain on attempting the chair raise test

E Pain on elbow flexion

- |   |   |
|---|---|
| A | Pain on pressure over the medial epicondyle |
| B | Pain on wrist flexion against resistance    |
| C | Pain on wrist pronation                     |
| D | Pain on attempting the chair raise test     |
| E | Pain on elbow flexion                       |

## Explanation

### Diagnosis of lateral epicondylitis

Tennis elbow is also known as lateral epicondylitis. Typical symptoms include pain just distal (5–10 mm) to the lateral epicondyle. Wrist extension or supination (but not flexion or pronation) against resistance with the elbow extended should provoke the patient's symptoms. The chair-raise test may also be useful in determining the diagnosis. The patient stands behind their chair and attempts to raise it by putting their hands on the top of the chair back and lifting. In patients with lateral epicondylitis, pain results over the lateral elbow.

Management involves physiotherapy, wearing a band around the elbow, steroid injection or lateral release surgery.



A 27-year-old man known to be HIV-positive presents to clinic with xerophthalmia, xerostomia, abdominal pain, weakness and exertional dyspnoea. He is noted to have bilateral parotid gland enlargement, hepatomegaly and a peripheral motor neuropathy. He is negative for rheumatoid factor and for antinuclear antibodies and SS-A and SS-B antibodies.

What is the most likely diagnosis?

- |   |   |
|---|---|
| A | Systemic lupus erythematosus              |
| B | Sjögren's syndrome                        |
| C | Lymphoma                                  |
| D | Diffuse infiltrative lymphocytic syndrome |
| E | Mixed connective tissue disease           |

## Explanation

### Diffuse infiltrative lymphocytic syndrome

Diffuse infiltrative lymphocytic syndrome (DILS) can present like Sjögren syndrome but extra glandular manifestations are common and it is rare for the patient to have positive autoantibodies. The weakness is due to a peripheral motor neuropathy. Aseptic meningitis and cranial nerve palsies can also occur. Lymphocytic interstitial pneumonitis is the most serious complication of DILS.

A 35-year-old man patient was referred from his GP because of recurrent genital ulcers and uveitis; he has had four recurrences in the last year. On examination the patient also has mouth ulcers.

What is the most likely diagnosis?

- |   |                        |
|---|------------------------|
| A | Sjögren's syndrome     |
| B | Behçet's disease       |
| C | Rheumatoid arthritis   |
| D | Systemic sclerosis     |
| E | Polymyalgia rheumatica |

## Explanation

### Behçet's disease

An international study group has proposed a set of diagnostic criteria based on data from 914 patients with the disease from 12 centres and seven countries. These criteria require the presence of recurrent oral ulcers and any two of the following: genital ulcers, defined eye lesions, defined skin lesions, a positive skin pathergy test.

Sjogren's is not usually associated with genital ulcers, there are not prominent features of arthritis here to suggest rheumatoid, and systemic sclerosis is associated with sclerodactyly and peripheral calcinosis. Polymyalgia is associated with shoulder and pelvic girdle pain.



You are explaining the common manifestations of systemic lupus erythematosus to a 32-year-old woman who has been diagnosed with the disease.

Which one of the following tissues are most commonly affected in this condition?

A Skin

B Lungs

C Heart and blood vessels

D Joints

E Kidneys

A	Skin
B	Lungs
C	Heart and blood vessels
D	Joints
E	Kidneys

## Explanation

### Joint involvement in SLE

Joint involvement in systemic lupus erythematosus (SLE) is the most common clinical feature (> 90%). Small joints are usually involved in a symmetrical fashion.

### Other systems

- + The skin is affected in 75% of cases and erythema in a butterfly distribution on the cheeks and across the bridge of the nose is characteristic.
- + Up to 60% of patients have lung involvement.
- + The heart and vascular system are affected in 25% of cases.
- + Clinical renal involvement occurs in approximately 30% of cases.

A 28-year-old woman presents with a 6-week history of weakness, especially on walking up stairs or rising from a chair. She has had a dry cough and shortness of breath. On examination she has a proximal myopathy and bibasilar crepitations. Investigations reveal: erythrocyte sedimentation rate (ESR) 74 mm in 1st hour, C-reactive protein (CRP) 32 mg/l, antinuclear antibody +, Jo-1 antibody positive. The creatine kinase is 5742 U/l, creatinine 231  $\mu$ mol/l. Urine dipstick shows +++ blood.

What is the likely cause of her renal failure?

A	Acute tubular necrosis
B	NSAID nephropathy
C	Malignancy
D	Amyloid
E	Acute glomerulonephritis

- |   |                          |
|---|--------------------------|
| A | Acute tubular necrosis   |
| B | NSAID nephropathy        |
| C | Malignancy               |
| D | Amyloid                  |
| E | Acute glomerulonephritis |

## Explanation

### Anti-Jo-1 syndrome

This woman has the anti-Jo-1 syndrome, which is characterised by polymyositis and lung fibrosis. Her creatine kinase level is very high and she has myoglobinuria (+++ blood on dipstick). Above levels of about 5000 U/l there is a risk of myoglobin crystallisation in the kidneys, which causes an acute tubular necrosis. The immediate management is to force a diuresis. It may be necessary to alkalinise the urine.



A 26-year-old man presents with a hot, swollen and tender right knee, the movement of which is severely limited by pain. He has recently returned from a holiday in Thailand and also has painful urethral discharge with pus and blood. There is no significant past medical history of note. On examination his BP is 135/72 mmHg, pulse is 78/min and regular. Temperature is 38.5°C. His right knee is swollen and hot with superficial erythema, and he is holding it in flexion because of ongoing pain.

Investigations;

Hb	13.1 g/dl
WCC	12.1 $\times 10^9/l$
PLT	201 $\times 10^9/l$
Na <sup>+</sup>	138 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	100 micromol/l
CRP	290 mg/l
Knee X-ray	unremarkable

Which of the following is the most appropriate next step?

A Aspiration of right knee

B Start IV Benzylpenicillin

C Start IV Ceftriaxone

D Blood cultures

E Start non-steroidals

## Explanation

The answer is Aspiration of right knee

It is clear that this man has a septic arthritis, as suggested by the monoarthritis with raised white count and CRP. The symptoms of urethritis suggest a sexually transmitted cause of which gonococcus is the most likely. Blind antibiotic therapy is not however indicated, and it is important to confirm the cause of his arthritis. Aspiration of synovial fluid is the optimal way to do this. IV Ceftriaxone is the antibiotic of choice because of penicillin resistance.

A 37-year-old woman with nephrotic syndrome has been on oral prednisolone for 6 years. She now presents with right-sided hip pain and a limping gait. Examination reveals limitation of abduction and internal rotation of the right thigh.

Which one of the following investigations would be most useful in this case?

A Joint fluid microscopy

B X-ray of the hip

C Blood culture

D Serum uric acid

E MRI of the hip



A Joint fluid microscopy

B X-ray of the hip

C Blood culture

D Serum uric acid

E MRI of the hip

## Explanation

### Early diagnosis of avascular necrosis of the femoral head

This patient most probably has suffered avascular necrosis of the femoral head because of her prolonged corticosteroid treatment. In early cases, the X-ray may be normal, but bone scintigraphy or magnetic resonance imaging will demonstrate the lesion.

A patient with systemic lupus erythematosus has uncontrolled hypertension during her pregnancy. She is in week 32 and has a blood pressure of 152/84 mmHg.

What is the most appropriate therapy?

A Warfarin

B Heparin

C Ramipril

D Labetalol

E Cyclophosphamide

A	Warfarin
B	Heparin
C	Ramipril
<b>D</b>	<b>Labetalol</b>
E	Cyclophosphamide

## Explanation

### SLE and hypertension in pregnancy

The goal of treatment for this woman with systemic lupus erythematosus (SLE) is to minimise symptoms and slow the progression of the disease. Symptoms should be treated as appropriate. Diuretics and angiotensin-converting enzyme (ACE) inhibitors should be avoided in pregnancy, but labetalol is considered a relatively safe option.

A 65-year-old woman with a 10-year history of rheumatoid arthritis, treated with meloxicam and methotrexate, presents with an acute swelling of her right knee. She is febrile (37.8 °C) with a warm, swollen right knee with an effusion. She has a mild neutrophilia and normochromic, normocytic anaemia. The C-reactive protein (CRP) is 70 mg/l and the erythrocyte sedimentation rate (ESR) is 65 mm in 1st hour.

Which one of the following represents the most appropriate management?

A	Add oral prednisolone to the present therapy
B	Aspirate the knee effusion and inject intra-articular depomedrone
C	Aspirate the knee effusion and send for microbiological analysis
D	Increase methotrexate to the maximal dose
E	Start a 6-week course of oral antibiotics



- |   |   |
|---|---|
| A | Add oral prednisolone to the present therapy                      |
| B | Aspirate the knee effusion and inject intra-articular depomedrone |
| C | Aspirate the knee effusion and send for microbiological analysis  |
| D | Increase methotrexate to the maximal dose                         |
| E | Start a 6-week course of oral antibiotics                         |

## Explanation

### A septic joint in rheumatoid arthritis

Septic arthritis must be excluded in this patient. Patients with rheumatoid arthritis have an increase risk of septic arthritis and the associated mortality in patients aged over 65 years is 20%. The knee should be aspirated under aseptic conditions and the synovial fluid sent in a sterile bottle for microbiological analysis. Inoculation of fluid into blood culture bottle increases the likelihood of culturing bacteria. It is important to inform the microbiologist that the patient is immunosuppressed because the incidence of atypical organisms will be increased. In addition, send synovial fluid for cytology and a white blood cell count.

A 47-year-old woman presents to the Rheumatology Clinic with severe rheumatoid arthritis for review. She has suffered from the disease for some 7 years and is managed with a combination of low-dose prednisolone and methotrexate. On examination she has evidence of joint disease affecting both hands, elbows and knees. Her investigations show: haemoglobin 11.3 g/dl, white cell count  $6.1 \times 10^9/l$ , platelets  $215 \times 10^9/l$ , erythrocyte sedimentation rate (ESR) 34 mm in 1st hour, sodium 139 mmol/l, potassium 4.8 mmol/l, creatinine 145  $\mu\text{mol/l}$ . You are reviewing possible targeted immunotherapies as the next treatment option.

Which one of the following is closely involved in the pathology of rheumatoid arthritis?

A	IL-10
B	IL-2
C	TNF-alpha
D	TGF-alpha
E	Epidermal growth factor

A	IL-10
B	IL-2
C	TNF-alpha
D	TGF-alpha
E	Epidermal growth factor

## Explanation

### Immunotherapy of rheumatoid arthritis

Elevated levels of tumour necrosis factor alpha (TNF- $\alpha$ ), interleukin 1 (IL-1), interleukin 6 (IL-6), transforming growth factor beta (TGF- $\beta$ ), fibroblast growth factor and platelet-derived growth factor have all been demonstrated in patients with rheumatoid arthritis. Elevated levels of TNF- $\alpha$  in particular have been demonstrated within the joint spaces of patients with active rheumatoid arthritis. Trials of anti-TNF- $\alpha$  agents have shown impressive results in rheumatoid arthritis and are prescribed for patients who have continued active disease despite introduction of a typical second-line agent.

A 74-year-old woman presents with left knee pain. She has a history of hypertension which is treated with indapamide 1.5 mg daily and is obese, with a body mass index (BMI) of 31 kg/m<sup>2</sup>. She looks well and her blood pressure is 135/82 mmHg. On examination the knee is unremarkable, but internal rotation of the left hip is limited by pain. Investigations show: haemoglobin 12.1 g/dl, white cell count  $5.2 \times 10^9/l$ , platelets  $192 \times 10^9/l$ , sodium 141 mmol/l, potassium 4.9 mmol/l, creatinine 110  $\mu\text{mol/l}$ , erythrocyte sedimentation rate (ESR) 10 mm in 1st hour. A left knee X-ray is normal.

Which one of the following is the most appropriate next investigation?

- |   |                           |
|---|---------------------------|
| A | MRI knee                  |
| B | Arthroscopy knee          |
| C | X-ray femur               |
| D | X-ray left hip and pelvis |
| E | Bone scan                 |



- |   |                           |
|---|---------------------------|
| A | MRI knee                  |
| B | Arthroscopy knee          |
| C | X-ray femur               |
| D | X-ray left hip and pelvis |
| E | Bone scan                 |

## Explanation

### Osteoarthritis of the hip

Patients with osteoarthritis of the hip may present with knee pain in the first instance, and particularly because limited internal rotation is a sign of hip arthritis. The white count is normal, as is erythrocyte sedimentation rate (ESR) so that there is nothing to indicate an infective or inflammatory cause here. Plain X-ray of the hip and pelvis is likely to provide evidence of the extent of joint destruction and inform the decision about the optimum time for hip replacement surgery. In the meantime, paracetamol with or without non-steroidal anti-inflammatory drugs would be the treatment of choice.

A 68-year-old man who is on a stable dose of warfarin therapy for an artificial aortic valve replacement comes to the Emergency Department. He has redness, swelling and pain over the first metatarsophalangeal joint of his right foot. On examination has appears to have acute gout. Investigations show: haemoglobin 11.9 g/dl, white cell count  $5.2 \times 10^9/l$ , platelets  $229 \times 10^9/l$ , sodium 140 mmol/l, potassium 4.5 mmol/l, creatinine 145  $\mu\text{mol/l}$ , international normalised ratio (INR) 2.9.

Which one of the following agents is the most appropriate treatment for his gout?

A Prednisolone

B Colchicine

C Diclofenac

D Allopurinol

E Indometacin

A	Prednisolone
B	Colchicine
C	Diclofenac
D	Allopurinol
E	Indometacin

## Explanation

### Treatment of acute gout

- + Prednisolone decreases polymorphonuclear cell activity and reduces capillary permeability and inflammation, therefore reducing pain and swelling in the joint during the acute period
- + Non-steroidal drugs such as indometacin and diclofenac should clearly be avoided in conjunction with warfarin as they may significantly increase the risk of bleeding
- + Colchicine is second line therapy, because non-steroidal drugs are the usual first-line treatment for acute gout, yet a number of drug surveillance experts have also collected case series suggesting that colchicine leads to elevations in the international normalised ratio (INR) in certain patients
- + Allopurinol can worsen symptoms when used acutely in the treatment of gout, so it should be avoided

A 35-year-old woman complains of bilateral stiff and painful joints in her hands and feet for the past 3 months. The stiffness lasts for more than an hour in the mornings. On examination, her fingers are swollen and stiff. Movement is painful.

Which test would be most likely to contribute to diagnosis in this case?

A X-ray of the hands and feet

B Serum uric acid levels

C Joint aspirate for crystals

D CRP levels

E Plasma rheumatoid factor



C	Joint aspirate for crystals
D	CRP levels
E	Plasma rheumatoid factor

## Explanation

### Diagnosis of rheumatoid arthritis

Diagnosis of rheumatoid arthritis relies on the clinical features. The American College of Rheumatology criteria (in use in the UK) are:

- + Morning stiffness >1 hour
- + Arthritis of three or more joints for 6 weeks or more
- + Arthritis of the hand joints and wrists
- + Symmetrical arthritis
- + Subcutaneous nodules
- + A positive serum rheumatoid factor
- + Typical radiological changes

Four or more criteria are necessary for diagnosis.

This patient already has the first four criteria. Rheumatoid factor is present in approximately 70% of cases. Only soft-tissue swelling may be visible on X-ray in early disease. Hence, testing for rheumatoid factor would be more relevant in this case.

A 19-year-old man presents to the Rheumatology Clinic with worsening pain and stiffness across his lower back and hips, which is particularly bad in the mornings. He has tried taking Ibuprofen and Paracetamol regularly with little effect. There is no past medical history of note. On examination his BP is 135/72 mmHg, pulse is 70/min and regular. There are no murmurs and his chest is clear, although expansion appears slightly reduced. He is tender over the sacroiliac joints bilaterally, and has limited lateral and forward flexion of his spine.

Which of the following is the optimal way to confirm the underlying diagnosis?

A	Autoantibody status
B	B27 status
C	ESR
D	MRI lumbar spine and pelvis
E	Whole spine X-ray

## Explanation

The answer is MRI lumbar spine and pelvis

The suspicion is that this patient has ankylosing spondylitis. Looking for sacroilitis is important with respect to confirming the diagnosis, and MRI is much more sensitive than plain X-ray in looking for early disease. Much later on in the disease vertebral bodies may become 'squared', syndesmophytes form between adjacent vertebrae, there is ossification of spinal ligaments and, in late disease, there may be complete fusion of the vertebral column. Whilst the vast majority of patients with AS are B27 positive, B27 negativity does not exclude the diagnosis. ESR is less specific for disease activity in AS than in other rheumatic diseases, and autoantibody status is unhelpful in AS.

A 30-year-old farmer presents with a history of myalgia, fatigability, occasional bouts of fever, depression and right knee joint pain for the past 6 months. On examination there is lymphadenopathy and hepatosplenomegaly. The *Brucella* agglutination titre is elevated fourfold.

Given the likely diagnosis, what treatment would be most helpful in this condition?

- |   |   |
|---|---|
| A | Intravenous benzylpenicillin monotherapy          |
| B | Erythromycin/co-amoxiclav/doxycycline combination |
| C | Doxycycline/rifampicin/gentamicin combination     |
| D | Amoxicillin monotherapy                           |
| E | Gentamicin/flucloxacillin combination             |



- |   |   |
|---|---|
| A | Intravenous benzylpenicillin monotherapy          |
| B | Erythromycin/co-amoxiclav/doxycycline combination |
| C | Doxycycline/rifampicin/gentamicin combination     |
| D | Amoxicillin monotherapy                           |
| E | Gentamicin/flucloxacillin combination             |

## Explanation

### Brucellosis

Brucellosis is commonly seen in people handling farm animals. The therapy with the lowest rate of relapse which is most easily obtainable is triple therapy with doxycycline, rifampicin and gentamicin in combination. Streptomycin may also be effective. Co-trimoxazole may be substituted as the third antibiotic with doxycycline and rifampicin to provide an all-oral regime.

Intravenous benzylpenicillin is useful in Lyme disease in the later stages. Intravenous penicillin or erythromycin is given in leptospirosis. Gentamicin is prescribed for tularaemia.

A 28-year-old man with ankylosing spondylitis presents with blood ++ and protein + in the urine. An ultrasound scan shows normal-sized kidneys.

A renal biopsy might reveal which one of the following features?

A	Apple-green birefringence in polarised light
B	Membranoproliferative glomerulonephritis
C	IgA deposition
D	Nephrolithiasis
E	Membranous glomerulonephritis

- |   |  |
|---|--|
| A | Apple-green birefringence in polarised light |
| B | Membranoproliferative glomerulonephritis     |
| C | <b>IgA deposition</b>                        |
| D | Nephrolithiasis                              |
| E | Membranous glomerulonephritis                |

## Explanation

### Nephropathy associated with ankylosing spondylitis

Three types of nephropathy are classically associated with ankylosing spondylitis:

- + AA amyloidosis, more common when the disease has been going on for many years. The kidneys are usually enlarged on ultrasound and biopsy shows amyloid - apple-green birefringence in polarised light.
- + Non-steroidal anti-inflammatory drug- (NSAID-) induced nephropathy.
- + IgA nephropathy, also common among young men in the absence of ankylosing spondylitis. It may be entirely asymptomatic or it can be associated with haematuria and hypertension.
- + In this case the presence of blood and protein most supports a diagnosis of IgA nephropathy and concurrent IgA deposition.

A 74-year-old woman complains of left knee pain that is exacerbated by weight bearing and ambulation. Examination of the knee reveals a small effusion (without warmth), bony enlargement and crepitus with flexion and extension of the knee. A diagnostic arthrocentesis is performed.

Which one of the following features of the arthrocentesis is an unusual finding in this case?

A	Pale yellow color
B	Good viscosity
C	Routine culture negative
D	White blood cell (WBC) count $800/\text{mm}^3$
E	Glucose $1.4 \text{ mmol/l}$



- |   |  |
|---|--|
| A | Pale yellow color                              |
| B | Good viscosity                                 |
| C | Routine culture negative                       |
| D | White blood cell (WBC) count $800/\text{mm}^3$ |
| E | Glucose $1.4 \text{ mmol/l}$                   |

## Explanation

### Synovial fluid analysis

Clinically, this patient has osteoarthritis of the left knee. Synovial fluid in patients with osteoarthritis is typically 'non-inflammatory', meaning that the leucocyte count is less than  $2000/\text{mm}^3$ .

A low level of glucose in the synovial fluid would not be found in this patient but is often found in septic arthritis of bacterial origin. Where the white blood cell count is above  $2000/\text{mm}^3$  empirical antibiotic therapy would usually be started, as any delay in initiation of therapy may result in severe joint damage.

A 25-year-old man presents with a 10-day history of low back pain and stiffness that is worse in the morning and relieved by exercise.

Which one of the following investigative findings would be seen earliest on an X-ray of the lower spine?

- |   |   |
|---|---|
| A | Blurring of the upper and/or lower vertebral rims at the thoracolumbar junction |
| B | Sclerosis of the sacroiliac joints  |
| C | Presence of syndesmophytes  |
| D | Fusion of spinal facet joints   |
| E | Calcification of intervertebral ligaments                                       |

A	Blurring of the upper and/or lower vertebral rims at the thoracolumbar junction
B	Sclerosis of the sacroiliac joints
C	Presence of syndesmophytes
D	Fusion of spinal facet joints
E	Calcification of intervertebral ligaments

## Explanation

### X-ray changes in ankylosing spondylitis

This patient most probably has ankylosing spondylitis.

### Early changes

The earliest radiological appearances in the spine are blurring of the upper and/or lower vertebral rims at the thoracolumbar junction (best seen on a lateral X-ray). This is caused by an enthesitis at the insertion of the intervertebral ligaments.

### Later changes

Persistent enthesitis causes bony spurs (syndesmophytes). Fusion and sclerosis of the sacroiliac joints and calcification of intervertebral ligaments occur at a later stage.

An 83-year-old man complains of neck pain that has been progressively increasing over the past month. An X-ray shows forward displacement of the fifth cervical vertebra.

What is the most probable cause of this condition?

- |   |  |
|---|--|
| A | Failure of fusion of the odontoid process with the axis                                    |
| B | Inflammatory softening of the transverse ligament of the atlas due to rheumatoid arthritis |
| C | Instability of the posterior facet joints due to osteoarthritis                            |
| D | Whiplash injury  |
| E | Osteoporosis   |



- |   |  |
|---|--|
| A | Failure of fusion of the odontoid process with the axis                                    |
| B | Inflammatory softening of the transverse ligament of the atlas due to rheumatoid arthritis |
| C | Instability of the posterior facet joints due to osteoarthritis                            |
| D | Whiplash injury  |
| E | Osteoporosis   |

## Explanation

### Cervical spondylolisthesis

This patient has cervical spondylolisthesis, where there is usually forward displacement of one vertebra upon another. The most common cause in this age group is osteoarthritis of the posterior intervertebral joints, which become unstable and permit vertebral displacement.

### Differential diagnosis

Congenital failure of fusion of the odontoid process with the axis is a rare condition and would also not involve the fifth cervical vertebra. There is no prior history of rheumatoid arthritis or whiplash injury. Osteoporosis would cause a crush fracture of vertebral bodies without displacement.

A 6-year-old girl presents with cold, painful lower extremities. On examination she is found to have a blood pressure of 180/120 mmHg in her right and left arms. The femoral pulse is found to be weak and the blood pressure in her lower limbs is 80/60 mmHg. An X-ray of the chest shows notching of the ribs along their lower borders.

What is the most likely diagnosis?

A Femoral artery thrombosis

B Coarctation of the aorta

C Raynaud's disease

D Takayasu's arteritis

E Cervical rib

B	Coarctation of the aorta
C	Raynaud's disease
D	Takayasu's arteritis
E	Cervical rib

## Explanation

### Painful extremities

- + The features are characteristic of coarctation of the aorta. Most patients are asymptomatic. Notching of the ribs is due to an increased collateral circulation.
- + Femoral artery thrombosis is usually unilateral and is unusual in this age group in the absence of a predisposing factor.
- + Raynaud's disease is the occurrence of Raynaud's phenomenon in the absence of any underlying disorder. This occurs predominantly in young women.
- + Takayasu's arteritis is an idiopathic vasculitis that affects the first few centimetres of the innominate, carotid and subclavian arteries and the adjacent portion of the aorta. The typical patient is a woman between the ages of 20 and 40 years. Peripheral pulses in the upper and lower limbs may be weak or absent. Involvement of the eyes and central nervous and cardiovascular systems leads to characteristic symptoms. The renal arteries are frequently involved, leading to hypertension.
- + A cervical rib may cause pain and numbness in the hand or forearm with weakness and muscle wasting. The radial pulse may be weak and the forearm cyanosed. X-rays will show the rib.

A middle-aged woman with a history of rheumatoid arthritis develops sudden swelling in one of her knees. The knee is hot and tender.

Which of the following is the most appropriate initial investigation in her case?

A Joint fluid microscopy and culture

B Joint fluid crystal examination

C Blood culture

D X-ray of the knee

E Test for rheumatoid factor



A	Joint fluid microscopy and culture
B	Joint fluid crystal examination
C	Blood culture
D	X-ray of the knee
E	Test for rheumatoid factor

## Explanation

### Septic arthritis

Septic arthritis may occur in a joint damaged by rheumatoid arthritis. This typically presents acutely with a painful, hot, tender, swollen joint, usually monoarticular. Joint fluid culture would be the most appropriate investigation in this case.

A 35-year-old patient complains of feeling unwell for the last 6 months. He has increased photosensitivity and a purplish-red rash around the eyes. On examination there is an erythematous scaly eruption over the extensor surfaces of his arms.

Which other concurrent disease would you suspect?

- |   |                   |
|---|-------------------|
| A | Hepatitis         |
| B | Diabetes mellitus |
| C | Haemochromatosis  |
| D | Malignancy        |
| E | Emphysema         |

D	Malignancy
E	Emphysema

## Explanation

### Underlying malignancy in dermatomyositis

This is dermatomyositis, showing a characteristic heliotrope rash that often precedes or accompanies muscle weakness. The heliotrope rash is a symmetrical, confluent, purple-red, macular eruption of the eyelids and periorbital tissue. Oedema may also be present. A significant proportion of adults with polymyositis and dermatomyositis have underlying malignancy, usually a carcinoma. The association with malignancy is stronger for adults with dermatomyositis, who die from cancer significantly more often than age-matched controls. Many types of malignancy have been reported in association with dermatomyositis, including lung, oesophageal, breast, colon and ovarian tumours. Among women with dermatomyositis, the risk of ovarian cancer is as much as 20 times greater than that of the general population.

### Investigation

Most patients diagnosed with primary polymyositis or dermatomyositis (children excepted) should undergo some surveillance for a disease-associated malignancy. This screening should be based on a careful history, physical examinations and the performance of a limited number of routine tests (eg chest radiography), in addition to age-appropriate cancer screening such as mammography and flexible sigmoidoscopy.

A 38-year-old man presents with lateral swelling and tenderness of both forearms. There is severe induration of the skin (*peau d'orange*) and bilateral carpal tunnel syndrome with flexion contractions of the fingers. He denies having Raynaud's phenomenon.

Investigations show: haemoglobin 13.1 g/dl, platelets  $360 \times 10^9/l$ , white cell count (WCC)  $7.8 \times 10^9/l$ , neutrophils  $4.3 \times 10^9/l$ , lymphocytes  $2.0 \times 10^9/l$ , eosinophils  $1.5 \times 10^9/l$ . Serum protein electrophoresis demonstrates hypergammaglobulinaemia.

What is the diagnosis?

- |   |                                |
|---|--------------------------------|
| A | Progressive systemic sclerosis |
| B | Eosinophilic fasciitis         |
| C | Eosinophilia myalgia syndrome  |
| D | Paraneoplastic syndrome        |
| E | Jaccoud's arthropathy          |



## Explanation

### Eosinophilic fasciitis

The characteristic findings in eosinophilic fasciitis are:

- + Swelling and tenderness of the forearms, with induration of the skin (*peau d'orange*)
- + Carpal tunnel syndrome
- + Flexion contractions of the fingers
- + Peripheral blood eosinophilia
- + Hypergammaglobulinaemia

There is an acute-phase response with elevated ESR and hypergammaglobulinaemia. Raynaud's does not occur. The diagnosis is confirmed by deep biopsy.

A 16-year-old school student complains of low back pain radiating to the back of his legs. There is no loss of sensation or movement. His erythrocyte sedimentation rate (ESR) is elevated and serum rheumatoid factor is negative. X-ray of the spine shows anterior squaring of the vertebrae.

What is the probable diagnosis?

- |   |                                    |
|---|------------------------------------|
| A | Lumbar disc prolapse with sciatica |
| B | Rheumatoid arthritis               |
| C | Spinal stenosis                    |
| D | Ankylosing spondylitis             |
| E | Paget's disease of bone            |

## Explanation

### Ankylosing spondylitis

The findings are suggestive of ankylosing spondylitis. Sacroiliitis is often the first abnormality, with irregularity and loss of cortical margins, widening of the joint space and subsequently marginal sclerosis, narrowing and fusion. Lateral views of the thoracolumbar spine might show anterior squaring of the vertebrae, which is caused by erosion and sclerosis of the anterior corners and periostitis of the waist of the vertebrae.

### Differential diagnosis

- + Rheumatoid arthritis is more common in women, with a peak onset in the fifth decade. It affects the peripheral joints (hips, knees, hands and feet).
- + There is a reduction in the joint space in cases of lumbar disc prolapse with sciatica and spinal stenosis (see below).
- + Spinal stenosis is a disorder of older age and commonly presents with pseudoclaudication, ie discomfort or pain in the legs on walking that is relieved by rest and by bending forwards.
- + Paget's disease is seldom diagnosed before the age of 40 years. The classic presentation is with bone pain, bone deformity, deafness and pathological fractures. The diagnosis is established by the finding of a raised serum alkaline phosphatase level associated with normal liver function tests.

A 57-year-old man on ciclosporin following a renal transplant suddenly develops severe pain, swelling and redness in his left knee.

Which one of the following investigations would be most helpful in providing a diagnosis?

- |   |                                       |
|---|---------------------------------------|
| A | Serum uric acid                       |
| B | Joint fluid microscopy and Gram stain |
| C | Blood culture                         |
| D | Serum creatinine                      |
| E | X-ray of the knee joint               |



- |   |                                       |
|---|---------------------------------------|
| A | Serum uric acid                       |
| B | Joint fluid microscopy and Gram stain |
| C | Blood culture                         |
| D | Serum creatinine                      |
| E | X-ray of the knee joint               |

## Explanation

### Diagnosis of septic arthritis

This patient most probably has septic arthritis as a consequence of his immunosuppressive therapy with ciclosporin. Aspiration of the joint fluid and Gram staining would establish the diagnosis. Blood cultures may not be positive in up to one-third of cases. X-ray of the joint would not reveal any abnormality, while serum urate and creatinine levels would be unaffected.

A 19-year-old man presents to his GP 1 month after returning from a holiday to Berlin. He complains of rectal discharge, pain and diarrhoea, and pain affecting his right knee. Additionally, he has pain and photosensitivity affecting both eyes, and hyperkeratotic, reddened skin on his palms and the soles of his feet.

On examination he appears to have conjunctivitis, keratoderma blennorrhagica and monoarthritis of his right knee. Investigations show: haemoglobin 12.1 g/dl, white cell count  $13.1 \times 10^9/l$ , platelets  $190 \times 10^9/l$ , sodium 141 mmol/l, potassium 4.0 mmol/l, creatinine 94  $\mu\text{mol/l}$ , erythrocyte sedimentation rate (ESR) 35 mm in 1st hour. Right knee aspirate showed no organisms.

Which one of the following is the most appropriate initial treatment for his arthritis?

- |   |  |
|---|--|
| A | Salazopyrine                             |
| B | Doxycycline                              |
| C | Prednisolone                             |
| D | Diclofenac                               |
| E | Intra-articular corticosteroid injection |

A	Salazopyrine
B	Doxycycline
C	Prednisolone
D	Diclofenac
E	Intra-articular corticosteroid injection

## Explanation

### Management of Reactive arthritis (previously Reiter syndrome) -

This man has reactive arthritis. Reactive arthritis may occur in conjunction with gastrointestinal or venereal infection, symptoms beginning around 1-3 weeks after the initial period of infection.

Non-steroidal anti-inflammatory drugs (NSAIDs) form the foundation of therapy, although here, where the patient has presented with monoarthritis, intra-articular therapy may remove the need for systemic NSAID therapy. The role of antibiotics is controversial, some commentators recommending their use because the origin of the disease is presumed to be an infectious agent, but others pointing out that their use does not shorten the course of the disease. Patients with prolonged systemic symptoms may be considered for oral corticosteroids or salazopyrine.

A 20-year-old Italian waiter has painful mouth and genital ulcers associated with arthralgia of his elbows and knees. On examination, tender, red, raised lesions are seen on both legs. He has had two such attacks in the past.

What is the most likely diagnosis?

- |   |                        |
|---|------------------------|
| A | Behçet's disease       |
| B | Enteropathic arthritis |
| C | Reiter syndrome        |
| D | Polyarteritis nodosa   |
| E | Gonococcal arthritis   |



# Explanation

## Behçet's disease

Behçet's disease is a vasculitis of unknown aetiology that characteristically targets venules. It is common in the Mediterranean region and in Japan, where there is a strong association with HLA B51. Oral ulcers occur in almost all cases. Genital ulcers are less common (60-80%). The usual skin lesions are erythema nodosum or acneiform lesions, but migratory thrombophlebitis and vasculitis also occur.

## Differential diagnosis

- + Enteropathic arthritis is an acute inflammatory oligoarthritis that occurs in 12% of people with ulcerative colitis and in 20% of people with Crohn's disease. Mouth ulcers, erythema nodosum and iritis can occur. Treatment of the underlying condition relieves the symptoms.
- + Reactive arthritis (formerly Reiter syndrome) is a triad of arthritis, conjunctivitis or uveitis and non-specific urethritis.
- + Ulceration is not a feature in gonorrhoea. Disseminated gonorrhoea can present with painful pustular skin lesions.
- + Mouth and genital ulceration is not a feature of polyarteritis nodosa.

A 58-year-old woman is admitted to hospital with a history of general muscle weakness of 12 months' duration. She also gives a history of pain in the small joints of her hand, which she has had for more than 18 months. In addition, there is a history of difficulty swallowing.

Examination is normal except for tenderness of her upper arms, there is no obvious synovitis affecting her hands. Her erythrocyte sedimentation rate (ESR) is 60 mm in 1st hour, her haemoglobin is 9.5 g/dl, and her mean corpuscular volume (MCV) and mean cell haemoglobin concentration (MCHC) are normal. Serum antinuclear antibodies and rheumatoid factor are positive. Creatine kinase is also raised.

What is the most likely diagnosis?

- |   |                                 |
|---|---------------------------------|
| A | Rheumatoid arthritis            |
| B | Sjögren syndrome                |
| C | Polymyalgia rheumatica          |
| D | Mixed connective tissue disease |
| E | Polymyositis                    |

# Explanation

## Polymyositis

Polymyositis is a disorder of the muscles characterised by necrosis of muscle fibres, together with regeneration and inflammation. Dermatomyositis is the name given to the condition when a rash accompanies polymyositis. This shows an increased incidence of carcinoma of the bronchus in men and of the ovary in women.

## Clinical features

It presents with proximal muscle weakness and wasting. Muscle pain and tenderness can occur in up to 50% of patients, but weakness is the main symptom. Arthralgia affecting the small joints of the hands can occur in about half of all patients, pre-dating the muscle weakness. Dysphagia due to oesophageal muscle spasm occurs in up to 50%. Raynaud's phenomenon is commonly seen.

## Diagnosis

Muscle enzymes (creatine phosphokinase and aldolase) are raised and can be used to monitor the disease. Electromyography (EMG) shows short polyphasic motor potentials, spontaneous fibrillation and high-frequency repetitive discharges. Patients have a raised erythrocyte sedimentation rate (ESR), a normocytic and normochromic anaemia, and positive rheumatoid factor and antinuclear antibodies.

## Treatment

Patients should be treated with prednisolone at a dose of 60 mg daily, reducing to a smaller maintenance dose. Physiotherapy to restore muscle strength can be helpful. Immunosuppressants such as methotrexate or azathioprine might be needed.



A patient with recently diagnosed systemic lupus erythematosus undergoes serum testing for antibody levels.

Which one of the following antibodies would be most indicative of severe systemic involvement?

- |   |                                     |
|---|-------------------------------------|
| A | Antinuclear antibodies              |
| B | Anticardiolipin antibodies          |
| C | Antinucleosome antibodies           |
| D | Rheumatoid factor                   |
| E | Anti double-stranded DNA antibodies |



- |   |                                     |
|---|-------------------------------------|
| A | Antinuclear antibodies              |
| B | Anticardiolipin antibodies          |
| C | Antinucleosome antibodies           |
| D | Rheumatoid factor                   |
| E | Anti double-stranded DNA antibodies |

## Explanation

### Antibodies in SLE

Double-stranded DNA (dsDNA) binding is specific for systemic lupus erythematosus (SLE) and is present in 70% of cases. However, its presence most often indicates severe systemic involvement (eg renal disease). Antinucleosome antibodies pre-date anti-dsDNA antibodies. Antinuclear antibodies are positive in almost all cases and are non-specific. Rheumatoid factor is positive in 25%, while anticardiolipin antibodies are present in 40% of patients.

A 44-year-old man presents with pain in his hips and lower back. Blood tests are unremarkable except for serum alkaline phosphatase, which is 1200 IU/l (normal range 45-105 IU/l). A plain X-ray shows osteolytic and osteosclerotic lesions.

What is the most common site of occurrence of this disease?

- A Skull
- B Tibia
- C Pelvis
- D Femur
- E Lumbar spine

- |   |              |
|---|--------------|
| A | Skull        |
| B | Tibia        |
| C | Pelvis       |
| D | Femur        |
| E | Lumbar spine |

## Explanation

### Paget's disease

This patient most probably has Paget's disease, as suggested by the results of the investigations. Between 60% and 80% of patients with radiologically identified Paget's disease are entirely asymptomatic. The disease may involve one bone or many. The condition commonly affects the pelvis and spine, particularly the lumbar spine, with a frequency of 30-75%. The sacrum is involved in 30-60% of cases and the skull in 25-65% of cases. The proximal long bones, especially the femur, are also affected frequently (25-35% of cases). Involvement of the shoulder girdle and proximal humerus is not uncommon. Though any bone may be affected, the fibula, ribs, and bones in the hands and feet are involved infrequently.

A 55-year-old man complains of a gritty sensation in his eyes and a dry mouth of several months' duration. He also has vague joint pains in his hands and feet. His wife mentions he is also dyspnoeic on exertion and cannot keep up with her during their walks.

What is the cause of his eye and mouth symptoms?

- |   |                                 |
|---|---------------------------------|
| A | Polymyositis                    |
| B | Polyarteritis nodosa            |
| C | Sjögren's syndrome              |
| D | Mixed connective tissue disease |
| E | Rheumatoid arthritis            |



## Explanation

### Sjögren syndrome

Sjögren syndrome is characterised by dry eyes and mouth and may be associated with arthralgia, Raynaud's phenomena, dysphagia and abnormal oesophageal motility, pulmonary diffusion defects and fibrosis. Respiratory symptoms may come from a combination xerotrachea, which manifests as a dry cough, interstitial lung disease or recurrent pneumonitis. Secondary Sjögren's may also occur in conjunction with other causes of fibrotic lung disease. Anti-Ro antibodies are found in over 70% of the patients with primary Sjögren syndrome.

A 32-year-old man is referred with bouts of low back pain waking him at night for about 6 months. The pain is localised to the lower lumbar region and the buttock. He has changed his job from working in a warehouse doing heavy lifting to clerical tasks. He has to wake himself an hour or two earlier in the mornings than he used to in order to loosen up so that he can get to work on time. His past medical history revealed a malignant skin melanoma that was surgically removed 2 years earlier.

What is the most probable diagnosis in this case?

- |   |   |
|---|---|
| A | Intervertebral disc prolapse and sciatica   |
| B | Spinal canal stenosis                       |
| C | Ankylosing spondylitis                      |
| D | Melanoma recurrence and spread to vertebrae |
| E | Osteomyelitis of the lower lumbar vertebra  |

# Explanation

## Ankylosing spondylitis

The character of the back pain implies inflammatory disease. Pain has persisted for over 3 months. He has noticed increasing back stiffness in the morning that improves during the day; and the pain is probably so severe at night that it prompts him to get up and become mobile to reduce the symptoms. The above features suggest an inflammatory nature of the pain, most probably ankylosing spondylitis.

Patients with ankylosing spondylitis generally present with back pain that is worse after rest and improves with exercise. The onset is typically insidious in a male under the age of 40.

## Differential diagnosis of back pain

Sciatica is the hallmark symptom of clinically significant disc herniation. It presents as sharp or burning pain that radiates down the posterior or lateral aspect of the leg to the ankle or foot (depending on the specific nerve root involved). The pain may be worsened by cough, Valsalva manoeuvre or by sneezing and is often accompanied by paraesthesia and numbness. Around 90% of mechanical causes of back pain last less than 8 weeks.

Spinal canal stenosis occurs in young people who have a congenitally narrowed lumbar spinal canal and also in elderly people with osteoarthritic spurring, chronic disc degeneration and facet-joint arthritis. The characteristic complaint is pain in the low back and gluteal region that is made worse by standing, walking or other activities that cause spinal extension. Other characteristics are relief by rest, especially by sitting or lying down, and by flexing the spine and hips. Symptoms are often made worse by walking and relieved by sitting down and resting. The symptoms can mimic vascular insufficiency and are sometimes referred to as 'pseudoclaudication.'



Back pain due to osteomyelitis is usually dull and often occurs in conjunction with low-grade fever and spasm over the paraspinal muscles. Tenderness to percussion over the involved vertebrae is common, but fever is absent in up to 50% of cases..

Malignant vertebral deposits often present with severe deep-seated pain that is worse at night and provoked by spine movement.

In malignant and infectious cases of backache the disease process is rapidly progressive and a serious compression fracture or an epidural abscess might ensue. The fact that this patient remained stable 6 months after presentation makes such a diagnosis unlikely, as does the fact that there is no mention of adjuvant therapy after his original melanoma surgery.

	<u>Mechanical back pain</u>	<u>Inflammatory back pain</u>
Onset	Acute	Insidious
Morning stiffness		+++
Effect of exercise	Makes it worse	Makes it better
Radiation	L5/S1 dermatomes	Diffuse
Neurological signs	Positive	Negative



A 37-year-old woman is referred to the Rheumatology Clinic with a 2-month history of pain, but no swelling, in her metacarpophalangeal and proximal interphalangeal (PIP) joints. She also complains of sore and gritty eyes. On direct questioning she has a dry mouth and dyspareunia. Investigations reveal: erythrocyte sedimentation rate (ESR) 80 mm in 1st hour, rheumatoid factor positive at 1:320, antinuclear antibodies 1:40, anti-Ro antibody positive, anti-La negative, C-reactive protein < 2 mg/l.

What is the most likely diagnosis?

- |   |                              |
|---|------------------------------|
| A | Rheumatoid arthritis         |
| B | Systemic lupus erythematosus |
| C | Primary Sjögren's syndrome   |
| D | Sarcoidosis                  |
| E | Dermatomyositis              |

- |   |                              |
|---|------------------------------|
| A | Rheumatoid arthritis         |
| B | Systemic lupus erythematosus |
| C | Primary Sjögren's syndrome   |
| D | Sarcoidosis                  |
| E | Dermatomyositis              |

## Explanation

### Sjögren syndrome

Sjögren syndrome is characterised by dry mucous membranes, especially affecting the eyes, mouth and vagina. It can exist as a primary condition or as a secondary entity (no other disease diagnosis). These patients may also suffer from arthralgia, which results in a non-deforming 'Jaccoud's arthropathy'.

Arthritis associated with joint erosion is uncommon. Hypergammaglobulinaemia is a frequent finding and explains the high ESR. This could be consistent with a diagnosis of sarcoidosis with anterior uveitis, but the positive anti-Ro antibody suggests Sjögren syndrome.

A 35-year-old woman presents with swollen and tender knee joints. There is a history of morning stiffness for the past 4 months and pain in the fingers while typing on her computer. On examination she has a temperature of 39 °C and ulcerated lower limbs, with hyperpigmentation. There are nodules over her elbows. Her neutrophil count is measured at  $0.7 \times 10^9/l$ .

What is the probable diagnosis?

- |   |                    |
|---|--------------------|
| A | Osteoarthritis     |
| B | Septic arthritis   |
| C | Gouty arthritis    |
| D | Felty's syndrome   |
| E | Reactive arthritis |

## Explanation

### Felty syndrome

Felty syndrome is a potentially serious condition that is associated with seropositive (rheumatoid-factor-positive) rheumatoid arthritis (RA). Around 1% of patients with RA develop Felty syndrome. It is characterised by the triad of RA, splenomegaly and granulocytopenia. Although many patients are asymptomatic, some develop serious and life-threatening infections secondary to granulocytopenia. Patients commonly present with bacterial infections of the skin (as in the present case) and respiratory tract. An aggressive level of immunosuppression directed at the underlying RA may contribute to the susceptibility to infection.

In reactive arthritis, the joint involvement follows a genitourinary or gastrointestinal infection. Septic arthritis is usually unilateral and acute in onset. The joint will be held in a flexed, immobile position. Movement of the joint will be minimal and excruciatingly painful.



A 74-year-old woman presents to the Rheumatology Clinic for an Emergency appointment. She has morning stiffness, particularly affecting her hips and shoulders, which lasts for up to the first hour of every morning. She has a past history of hypertension for which she takes ramipril and atorvastatin, but nil else of note. On examination she has stiffness and movement restricted by pain affecting both her hips and shoulders. Her BP is 149/82 mmHg, there are no other abnormal findings.

Investigations;

Hb	12.9 g/dl
WCC	$9.1 \times 10^9/l$
PLT	$192 \times 10^9/l$
ESR	72 mm/1 <sup>st</sup> hour
Na <sup>+</sup>	138 mmol/l
K <sup>+</sup>	4.5 mmol/l
Creatinine	139 micromol/l
Rheumatoid factor	negative
Anti-nuclear antibody	negative
USS shoulders	Subdeltoid bursitis and biceps tendon tenosynovitis

Which of the above features is most consistent with a diagnosis of polymyalgia rheumatica versus another problem?

A

ESR 72 mm/1<sup>st</sup> hour

B

USS appearance

C

Creatinine 139 micromol/l

D

Rheumatoid factor negativity

E

Anti-nuclear antibody negativity

## Explanation

The answer is USS appearance -

Subdeltoid bursitis and biceps tendon tenosynovitis is typical of polymyalgia rheumatica (PMR) and when found is strongly supportive of the diagnosis. Whilst the elevated ESR is strongly supportive of a diagnosis of PMR, it is relatively non-specific. Rheumatoid factor negativity and anti-nuclear antibody negativity reduce the probability of underlying rheumatoid arthritis or other connective tissue disease, but don't rule them out completely. Her creatinine of 139 micromol/l may well be related to hypertensive renal disease.

A 48-year-old woman presents to the clinic for review with a diagnosis of simple obesity. Despite a BMI of 33 she does not have diabetes mellitus, hypertension or dyslipidaemia. She takes no regular medication. On examination her BP is 135/82 mmHg; pulse is 75/min and regular. You confirm that her BMI is 33; there are no other findings of significance and routine bloods are normal.

Which of the following is she most likely to suffer from?

- |   |                      |
|---|----------------------|
| A | Osteoporosis         |
| B | Osteomalacia         |
| C | Osteoarthritis       |
| D | Paget's disease      |
| E | Rheumatoid arthritis |



## Explanation

The answer is Osteoarthritis -

The risk of osteoporosis is increased in obese patients with Type 2 diabetes, although in obese individuals without diabetes, bone mineral density is actually increased. There is no link between obesity and increased risk of osteomalacia, Paget's or rheumatoid arthritis. The risk of osteoarthritis of the knees and hips in particular is significantly increased because of increased wear and tear related to elevated BMI.

A 24-year-old man has been complaining of back pain for over 12 months.

Which one of the following features is most specific for ankylosing spondylitis?

- A Limited lumbar spine motion on physical examination
- B Back stiffness worsening as the day wears on
- C Bilateral erosion of sacroiliac joints on X-ray
- D Presence of HLA-B27 antigen on tissue typing
- E Tenderness bilaterally in the lower lumbar area

- |   |  |
|---|--|
| A | Limited lumbar spine motion on physical examination    |
| B | Back stiffness worsening as the day wears on           |
| C | <b>Bilateral erosion of sacroiliac joints on X-ray</b> |
| D | Presence of HLA-B27 antigen on tissue typing           |
| E | Tenderness bilaterally in the lower lumbar area        |

## Explanation

### Ankylosing spondylitis

Bilateral sacroiliac erosion on X-ray is the feature most suggestive of ankylosing spondylitis. Limited lumbar spine motion or tenderness can occur with other painful back conditions such as disc disease or muscle strain. The back stiffness in ankylosing spondylitis is worse in the morning and improves as the day wears on. HLA-B27 is also found in normal individuals.

A 55-year-old woman presents complaining of tiredness, arthralgia, muscle weakness, weight gain and depression. Blood tests show mild normocytic normochromic anaemia with increased serum creatine kinase levels 320 U/l (24-170). Her pulse is 48 beats per minute and her BP is 140/90 mmHg.

Given the suspected clinical diagnosis, which of the following blood tests would be most useful in the diagnosis of this condition?

A	Serum aspartate transferase
B	Serum alkaline phosphatase
C	Erythrocyte sedimentation rate
D	Serum TSH
E	Serum antinuclear antibodies



- |   |                                |
|---|--------------------------------|
| A | Serum aspartate transferase    |
| B | Serum alkaline phosphatase     |
| C | Erythrocyte sedimentation rate |
| D | Serum TSH                      |
| E | Serum antinuclear antibodies   |

## Explanation

### Aches and malaise in middle age

- + Relative bradycardia, weight gain, malaise, arthralgia, mildly elevated CK and depression are features of hypothyroidism. Hence TSH assay looking for primary hypothyroidism is the investigation of choice
- + Polymyalgia rheumatica shows many similarities, but weight loss rather than weight gain is seen in this condition. Bradycardia is not a feature of polymyalgia rheumatica
- + General malaise, weight loss and fever occur during the acute phase of adult polymyositis. The major feature in adult polymyositis is progressive proximal muscle weakness and wasting. Pain and tenderness seen in up to 1/3<sup>rd</sup> of patients, particularly on muscle palpation

A 59-year-old chronic smoker with long-standing diabetes mellitus is admitted to hospital with a lung infection. He is found to have a grossly swollen and deformed right ankle with tingling and numbness in the area.

What is the probable diagnosis?

- |   |                            |
|---|----------------------------|
| A | Candidiasis                |
| B | Mononeuritis multiplex     |
| C | Charcot's joint            |
| D | Thromboangiitis obliterans |
| E | Septic arthritis           |

## Explanation

### Charcot's joint

Charcot's deformity arises in weight-bearing joints (mainly the ankles) and may be caused by neurovascular changes rather than simple neurotrauma. It is most commonly associated with chronic sensory neuropathies such as those found in diabetes mellitus, tertiary syphilis and syringomyelia.

A 67-year-old man presents to the Rheumatology Clinic for review. He is suffering from increasingly severe pain affecting his left hip and pelvis. Although his GP has prescribed regular Ibuprofen this has not significantly impacted on his symptoms and he is now finding it difficult even to walk a few metres to the local bus stop. He has a past medical history of hypertension, treated with Lisinopril and Indapamide, but nil else of note. On examination his BP is 138/82 mmHg; pulse is 77/min and regular. His BMI is 25 kg/m<sup>2</sup>. Flexion and external rotation of the left hip is severely limited because of pain and stiffness.

Investigations;

Hb	13.1 g/dl
WCC	8.5 x10 <sup>9</sup> /l
PLT	201 x10 <sup>9</sup> /l
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	102 micromol/l
Glucose	5.1 mmol/l
Ca <sup>++</sup>	2.2 mmol/l
ALP	479 U/l
PO <sub>4</sub> <sup>-</sup>	1.1 mmol/l
Urine	negative for blood and protein

Which of the following is the most likely diagnosis?



Which of the following is the most likely diagnosis?

- |   |                      |
|---|----------------------|
| A | Multiple myeloma     |
| B | Osteoarthritis       |
| C | Osteomalacia         |
| D | Paget's disease      |
| E | Secondary malignancy |

## Explanation

The answer is Paget's disease -

The pain localised to the left hip and pelvis, coupled with a rise in alkaline phosphatase, normal calcium and phosphate, in the absence of other symptoms or signs, is consistent with a diagnosis of Paget's disease. Plain X-ray of the hip and pelvis is likely to show areas of osteolysis and sclerosis and joint deformity consistent with a diagnosis of Paget's. Bone scintigraphy shows areas of increased uptake of the isotope where there is Paget's activity. Bisphosphonates are the management of choice.

A 54-year-old woman comes to the Emergency Department for review. She has recently been diagnosed with partial epilepsy and began treatment with Carbamazepine 3 months earlier. Over the past 4 weeks she has begun to develop joint pains, muscle aches and night sweats, mucosal ulcers and plaque like erythematous lesions over the surface of her skin. On examination her BP is 132/82 mmHg; pulse is 72/min and regular. There are no murmurs and her chest is clear. You confirm there is evidence of a small joint polyarthritis, and erythematous plaques over the upper body.

Investigations;

Hb	12.5 g/dl
WCC	$9.2 \times 10^9/l$
PLT	$157 \times 10^9/l$
Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	4.1 mmol/l
Creatinine	95 micromol/l
ESR	65 mm/1 <sup>st</sup> hour
Urine	blood and protein negative

Which of the following is most likely to be positive?

Which of the following is most likely to be positive?

- |   |                    |
|---|--------------------|
| A | Anti-CCP           |
| B | Anti-dsDNA         |
| C | Anti-ssDNA         |
| D | Anti-smooth muscle |
| E | Rheumatoid factor  |



## Explanation

The answer is Anti-ssDNA -

The clinical picture here is typical of drug-induced lupus (DLE), which is recognised to occur in conjunction with Carbamazepine, with symptoms appearing anywhere from 3 weeks to 2 years after initiation of the offending agent. Anti-CCP and rheumatoid factor are more associated with rheumatoid arthritis, anti-dsDNA with systemic lupus erythematosus and anti-smooth muscle antibodies with autoimmune hepatitis. Symptoms of DLE resolve within a short period of discontinuing the responsible medication.

Agents recognised to cause drug-induced lupus are listed below:

Antiarrhythmics - Procainamide and Quinidine

Antibiotics - Minocycline, Isoniazid, Rifabutin

Antifungals - Griseofulvin and Voriconazole

Anticonvulsants - Valproate, Ethosuximide, Carbamazepine, and hydantoins

Antihypertensives - Hydralazine, Methyldopa, and Captopril

Anti-inflammatories - Penicillamine and Sulfasalazine

Antipsychotics - Chlorpromazine

Cholesterol-lowering agents - Lovastatin, Simvastatin, Atorvastatin, and Gemfibrozil

Biologics - Interleukins (eg, IL-2), interferons (eg, alfa, beta, gamma), TNF- $\alpha$  (Etanercept,

Infliximab, Adalimumab), and Rituximab

Inhalers - Tiotropium bromide inhaler

Chemotherapy agents - Docetaxel, Paclitaxel, Cabazitaxel, Gemcitabine

A college student complains of painful mouth ulcers associated with pain and swelling in both hands. She has had several episodes of vasospasm in her fingers, with pallor, cyanosis and subsequent redness caused by reactive hyperaemia. Blood tests reveal antibodies to double-stranded DNA (anti-dsDNA) and antinuclear antibodies.

What is the most likely diagnosis?

- |   |                              |
|---|------------------------------|
| A | Behçet's syndrome            |
| B | Wegener's granulomatosis     |
| C | Systemic lupus erythematosus |
| D | Systemic sclerosis           |
| E | Sjögren's syndrome           |

# Explanation

## Systemic lupus erythematosus

The diagnosis of systemic lupus erythematosus (SLE) is established by the identification of antinuclear (ANA) and anti-double-stranded DNA antibodies. Raynaud's phenomenon is common in SLE and is likely to be idiopathic in this young woman.

Features of systemic sclerosis can include calcinosis of subcutaneous tissues, Raynaud's phenomenon, disordered oesophageal motility, sclerodactyly and telangiectasia.

A 43-year-old man with a past history of hypothyroidism presents with a 3-month history of pain and stiffness in the joints of his hands and feet. He also gives a history of dyspnoea, which started 6 weeks ago. Examination shows swollen hand joints and signs of a right pleural effusion. A diagnosis of rheumatoid arthritis is made.

Which one of the following is characteristic of a rheumatoid pleural effusion?

- |   |  |
|---|--|
| A | It is a transudate   |
| B | It has a low glucose level                                     |
| C | Long-standing rheumatoid effusions have low cholesterol levels |
| D | It has a high pH   |
| E | It should be treated by decortication                          |



A	It is a transudate
B	It has a low glucose level
C	Long-standing rheumatoid effusions have low cholesterol levels
D	It has a high pH
E	It should be treated by decortication

## Explanation

### Rheumatoid pleural effusion

Up to 5% of patients with rheumatoid arthritis develop pleural effusions at some stage. Pleural effusions are more common in men. These effusions are exudates and typically have a low pH ( $< 7.2$ ), a high lactic acid dehydrogenase (LDH) level and a low glucose level. Rheumatoid arthritis is unlikely to be the cause of an effusion if the glucose level in the fluid is over 1.6 mmol/l. Large amounts of cholesterol can accumulate in long-standing rheumatoid pleural effusions.

**Treatment:** Patients should be treated initially with non-steroidal anti-inflammatory drugs (NSAIDs). Decortication should be considered in patients with thickened pleura who are symptomatic with dyspnoea.

A 61-year-old man presents with a 2-month history of pain affecting his shoulders, knees, wrists and hands. He describes early morning stiffness lasting for 1 hour. There is swelling of his left ankle and second and third metacarpophalangeal (MCP) joints on both hands. He has lost 3 kg in weight and has a low-grade pyrexia.

Investigations reveal: normochromic normocytic anaemia with haemoglobin 9.7 g/dl, erythrocyte sedimentation rate (ESR) 56 mm in 1st hour, C-reactive protein (CRP) 21 mg/l, rheumatoid factor and antinuclear antibody both negative, creatine kinase 163 U/l.

What is the most likely diagnosis?

- |   |                         |
|---|-------------------------|
| A | Paraneoplastic syndrome |
| B | Polymyalgia rheumatica  |
| C | Reiter's syndrome       |
| D | Rheumatoid arthritis    |
| E | Temporal arteritis      |

- |   |                         |
|---|-------------------------|
| A | Paraneoplastic syndrome |
| B | Polymyalgia rheumatica  |
| C | Reiter's syndrome       |
| D | Rheumatoid arthritis    |
| E | Temporal arteritis      |

## Explanation

### Diagnosis of rheumatoid arthritis

These findings satisfy the American College of Rheumatology (ACR) criteria for rheumatoid arthritis. A positive rheumatoid factor is not necessary and systemic features such as pyrexia and weight loss can occur without there being an underlying malignancy.

An 8-year-old Japanese boy complains of pain in his elbows and knees, with swelling of his hands and feet. On examination, his temperature is 39 °C, pulse 120/minute and blood pressure 100/60 mmHg. His tongue is red in colour. Conjunctival congestion and cervical lymphadenopathy are noted.

What is the most likely diagnosis?

- |   |                                      |
|---|--------------------------------------|
| A | Kawasaki's disease                   |
| B | Sjögren's syndrome                   |
| C | Diffuse cutaneous systemic sclerosis |
| D | Behçet's syndrome                    |
| E | Felty's syndrome                     |



# Explanation

## Kawasaki disease

Kawasaki disease is an acute systemic disorder of childhood that predominantly occurs in Japan (800 cases per million in children under the age of 5 years). The causative factor is not known, but *Mycoplasma* and HIV infection may be associated in some cases.

Principal clinical features:

- + Fever persisting for more than 5 days
- + Bilateral conjunctival congestion
- + Non-purulent cervical lymphadenopathy
- + Polymorphous rash
- + Arthralgia
- + Palmar erythema
- + Strawberry tongue

## Differential diagnosis

Diffuse cutaneous systemic sclerosis is associated with skin, renal and gut involvement. Arthralgia, morning stiffness and flexor tenosynovitis are common. Behçet syndrome is a vasculitis of unknown aetiology that characteristically targets venules. Felty syndrome is the association of splenomegaly and neutropenia with rheumatoid arthritis. Lymphadenopathy is common and there is a predisposition to recurrent infections.

A 39-year-old woman presents with episodes of tingling, numbness and burning of the fingers of both hands over the past year. Her doctor thinks it could be Raynaud's phenomenon.

With which disease is this phenomenon most often seen?

- |   |                              |
|---|------------------------------|
| A | Systemic sclerosis           |
| B | Systemic lupus erythematosus |
| C | Cryoglobulinaemia            |
| D | Polyarteritis nodosa         |
| E | Adult polymyositis           |

A	Systemic sclerosis
B	Systemic lupus erythematosus
C	Cryoglobulinaemia
D	Polyarteritis nodosa
E	Adult polymyositis

## Explanation

### Raynaud's phenomenon

Raynaud's phenomenon is seen in almost 100% cases of systemic sclerosis and can precede the onset of the full-blown disease by many years. It is less common in systemic lupus erythematosus (SLE). The condition may also be seen in other disorders, such as polyarteritis nodosa, cryoglobulinaemia and adult polymyositis.

A 32-year-old woman is referred to the Rheumatology Clinic for review. She has a history of small joint polyarthritis affecting her elbows, knees, wrists, and the PIP joints of both hands. She is rheumatoid factor and anti-CCP antibody positive. Her GP has attempted therapy with Naproxen for the past 8 weeks with little relief, and her symptoms pre-date first presentation to the GP by at least 6 weeks. Examination reveals evidence of active synovitis.

Investigations:

Hb	12.8 g/dl
WCC	$7.2 \times 10^9/\text{l}$
PLT	$345 \times 10^9/\text{l}$
Na <sup>+</sup>	138 mmol/l
K <sup>+</sup>	4.3 mmol/l
Creatinine	95 micromol/l
ESR	75 mm/1st hour



Which of the following is the most appropriate next step?

- A Addition of Etanercept
- B Corticosteroids and Methotrexate in combination
- C High dose corticosteroids as monotherapy
- D Methotrexate
- E Switch of NSAID to Ibuprofen

## Explanation

The answer is Corticosteroids and Methotrexate in combination -

Early and aggressive therapy with respect to rheumatoid arthritis is now well recognised to limit joint damage over the longer term. It is also recognised that combination therapy with corticosteroids and a second line agent such as methotrexate has a greater chance of achieving clinical remission. High dose corticosteroids alone and methotrexate alone are also more likely to be associated with dose related adverse events. Switching the NSAID will have little or no chance of preventing permanent joint damage, and according to NICE biologicals are not indicated until the failure of conventional DMARDS has occurred (in contrast to ankylosing spondylitis where a recommendation is made to move to biologicals after failure of two NSAIDs).

<http://www.nice.org.uk/guidance/CG79>

A 22-year-old student with ankylosing spondylitis has increasing back pain and early morning stiffness.

What treatment would you advise?

- |   |                               |
|---|-------------------------------|
| A | Paracetamol                   |
| B | Colchicine                    |
| C | Laminectomy and spinal fusion |
| D | Oral prednisolone             |
| E | Oral NSAIDs                   |

- |   |                               |
|---|-------------------------------|
| A | Paracetamol                   |
| B | Colchicine                    |
| C | Laminectomy and spinal fusion |
| D | Oral prednisolone             |
| E | Oral NSAIDs                   |

## Explanation

### Treatment of ankylosing spondylitis

Non-steroidal anti-inflammatory drugs (NSAIDs) are often effective in relieving the symptoms of ankylosing spondylitis. Paracetamol will not help, while colchicine can cause vomiting and severe diarrhoea. Oral steroids should be avoided. Total hip arthroplasty has largely obviated the need for difficult spinal surgery in those with advanced deformity.



A 63-year-old woman presents with pain and marked swelling affecting her proximal interphalangeal, distal interphalangeal and carpometacarpal joints on both hands. The episodes of pain and swelling respond to non-steroidal anti-inflammatory drugs (NSAIDs). Plain radiographs demonstrate erosions in a gull-wing pattern but no periarticular osteoporosis. A full blood count is normal, rheumatoid factor and antinuclear antibodies are negative. The erythrocyte sedimentation rate (ESR) is 29 mm in 1st hour and the C-reactive protein (CRP) is 10 mg/l.

What is the most likely diagnosis?

- |   |                        |
|---|------------------------|
| A | Erosive osteoarthritis |
| B | Polyarticular gout     |
| C | Psoriatic arthritis    |
| D | Rheumatoid arthritis   |
| E | Seronegative arthritis |

# Explanation

## Erosive osteoarthritis

This scenario describes the classic features of erosive inflammatory osteoarthritis. The gull-wing or inverted-T pattern of erosions is typical of erosive inflammatory osteoarthritis. It is commonly confused with rheumatoid arthritis but of note there is no juxta-articular osteoporosis.

Were this to be inflammatory arthritis, then it would be expected that both the ESR and the CRP would be significantly abnormal, as you can see in this case both are normal or just above the normal range.

A 22-year-old woman presents with red scaly plaques on her elbows, knees, lower back and scalp. She also has pitting and yellow-brown discoloration of her nails and painful deformed finger and toe joints.

Given the likely clinical diagnosis, what would be the most appropriate treatment, taking current UK guidelines into account?

- |   |                 |
|---|-----------------|
| A | NSAIDs          |
| B | Sulfasalazine   |
| C | Methotrexate    |
| D | Corticosteroids |
| E | Etanercept      |

A	NSAIDs
B	Sulfasalazine
C	Methotrexate
D	Corticosteroids
E	Etanercept

## Explanation

### Treatment of severe psoriatic arthropathy

- + This patient has psoriasis with nail and joint involvement. As the disease is severe, methotrexate or ciclosporin may be given to control the skin lesions and arthritis.
- + Etanercept (fully humanised tumour necrosis factor alpha, TNF- $\alpha$  inhibitor) has been found to be highly effective in the treatment of severe skin and joint disease, but it is only recommended when conventional disease-modifying agents have failed.
- + Non-steroidal anti-inflammatory drugs (NSAIDs) and/or analgesics help the pain but they can occasionally exacerbate the skin lesions.
- + Sulfasalazine is prescribed for milder, polyarticular cases.
- + Corticosteroids taken orally may destabilise the skin disease and are best avoided.



A 65-year-old woman who lives alone complains of increasing pain in her left knee and episodes of the joint 'giving way'. She is no longer able to climb stairs. Valgus deformity with instability is also noted. She currently takes 6-8 Co-codamol 30/500 tablets per day.

Which of the following treatments would be most appropriate for her?

- |   |                                    |
|---|------------------------------------|
| A | Oral NSAIDs                        |
| B | Intra-articular steroid injections |
| C | Joint replacement                  |
| D | Physiotherapy                      |
| E | Hormone replacement therapy        |

- |   |                                    |
|---|------------------------------------|
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## Explanation

### Management of osteoarthritis

Disabling osteoarthritis in the elderly who live alone requires definitive treatment so that their independence is not curtailed. Joint replacement would be the best choice in this case.

A 52-year-old man presents with an acutely painful and red right big toe. His uric acid level is 0.6 mmol/l (normal range 0.23–0.46 mmol/l).

What is the most common cause of hyperuricaemia in gout?

A	Increased production of uric acid
B	Inborn error of metabolism
C	Decreased removal of uric acid by the liver
D	Impaired renal excretion of uric acid
E	Decreased faecal excretion of uric acid

- |   |   |
|---|---|
| A | Increased production of uric acid           |
| B | Inborn error of metabolism                  |
| C | Decreased removal of uric acid by the liver |
| D | Impaired renal excretion of uric acid       |
| E | Decreased faecal excretion of uric acid     |

## Explanation

### Hyperuricaemia in gout

Around 90% of patients with gout have impaired renal excretion of urate, 10% exhibit increased production, while less than 1% have an inborn error of metabolism that leads to purine overproduction. The liver is not involved in urate removal. Although one-third of uric acid is removed in the faeces, faecal removal is not associated with hyperuricaemia.



A 27-year-old woman with systemic lupus erythematosus (SLE) complains of central chest pain which is worse on inspiration. Auscultation of her heart reveals no abnormality. You suspect, however, that her symptoms are due to cardiac involvement by SLE.

What is the most likely pathology?

- |   |                       |
|---|-----------------------|
| A | Myocarditis           |
| B | Aortic valve lesions  |
| C | Cardiomyopathy        |
| D | Pericarditis          |
| E | Libman-Sacks syndrome |

- |   |                       |
|---|-----------------------|
| A | Myocarditis           |
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## Explanation

### Cardiac involvement in SLE

The heart is involved in 25% of patients with systemic lupus erythematosus (SLE). Pericarditis with small pericardial effusions detected by echocardiography is common. A mild myocarditis also occurs, giving rise to arrhythmias. Aortic valve lesions and cardiomyopathy occur rarely. A non-infective endocarditis involving the mitral valve (Libman-Sacks syndrome) is very rare.

A 20-year-old man is seen in the clinic with a rash over his buttocks and lower legs and pain and swelling in both knees. Two weeks earlier he had an upper respiratory tract infection. His blood pressure is 170/100 mmHg. Routine blood tests are unremarkable except for raised IgA levels and an ESR of 62 mm/1<sup>st</sup> hour. Urinalysis shows evidence of proteinuria.

What is the most likely diagnosis?

- |   |                                      |
|---|--------------------------------------|
| A | Henoch-Schönlein purpura             |
| B | Diffuse cutaneous systemic sclerosis |
| C | Polyarteritis nodosa                 |
| D | Microscopic polyangiitis             |
| E | Haemolytic-uraemic syndrome          |

## Explanation

### Henoch-Schönlein purpura

This patient has Henoch-Schönlein purpura, characterised by raised IgA levels causing IgA nephropathy. It is a small-vessel vasculitis that usually occurs in children and young adults. End-stage renal failure is rare in this condition.

### Differential diagnosis

Haemolytic-uraemic syndrome usually occurs following a gastrointestinal infection and bloody diarrhoea caused by *Escherichia coli* (O157 serotypes), which produces a verotoxin. There is severe microangiopathy, anaemia and thrombocytopenia progressing to acute renal failure.

Microscopic polyangiitis presents with rapidly progressive glomerulonephritis which is often associated with alveolar haemorrhage. Cutaneous and gastrointestinal involvement similar to that in polyarteritis nodosa is common. Less common features are neuropathy and pleural effusions (15%). These patients are also positive for perinuclear antineutrophil cytoplasmic antibody (pANCA).

The clinical features are not suggestive of diffuse cutaneous systemic sclerosis.